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USSR Report

LIFE SCIENCES

BIOMEDICAL AND BEHAVIORAL SCIENCES

(FOUO 1/80)

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CONTENTS (Continued)

I. ADVANCED BIOTECHNOLOGY

UDC: 663.18:576.8.095.3(047)

RECOVERY OF MICROBIAL METABOLITES

Moscow POLYCHENIYE MIKROBNYKH METABOLITOV Seriya P. Obshchiye voprosy mikrobiologicheskoy promyshlennosti, Obzor· in Russian 1979 annotation page and pp 1-17

[Annotation (by Prof A. M. Bezborodov, doctor of biological sciences) and introduction to survey "Recovery of Microbial Metabolites. Series P: General Problems of the Microbiological Industry," published by the Main Administration for the Microbiological Industry under the USSR Council of Ministers, Department of Scientific and Technical Information, Technical and Economic Research of the Microbiological Industry]

[Text] Annotation

This survey furnishes an analysis of the data in the literature pertaining to recovery of microbial concentrates, treatment of culture fluids, as well as biomasses for isolation of products of secondary synthesis. Chemical, ion-exchange, diaphragm and other processes for isolation of metabolites are discussed. Examples are furnished on how special-purpose products (amino acids, enzymes, etc.) are recovered.

This survey is intended for bioengineers, chemists, technologists and biochemists at institutes and enterprises of the microbiological industry, as well as employees of the ministries of the medical, food and chemical industries.

The survey is 72 pages long; there are 4 tables and 2 figures; bibliography lists 278 items.

Introduction

The biomasses and microbial metabolites--products of microbiological synthesis that are produced in various forms by enterprises of the microbiological, medical, chemical (biochemical reagents and certain drugs), food industries and Ministry of Agriculture--are very important to development of the national economy [1-4]. Wide use is made of the following prepared forms: inactivated and live biomasses (feed yeast, baker's yeast,

bacterial fertilizers and others); concentrates (mainly for agriculture) obtained by dehydration or partial purification of culture fluid; extracellular and intracellular purified metabolites used mainly as biochemical reagents and drugs, as well as to balance feed and foods (amino acids, vitamins, etc.).

Thus, as compared to 1966, production of feed yeast in 1976 in our country increased by 6.6 times, that of feed antibiotics by 6.2 times, enzyme products by 14.8 times and lysine by 42.6 times. Production of microbiologicals is also developing in other countries [5].

Preparation of nutrient media, inoculums, other prefermentation operations, as well as fermentation proper are similar for all finished products, and they have been described rather well in previous surveys [6-11]. Biomass is recovered at yeast plants and other enterprises.

There must be broad introduction into biotechnology of new and highly efficient methods of recovering biologicals, as well as creative use of the classical methods, in order to expand significantly the microbiological industry. Figure 1 schematically illustrates the possible directions of recovery of products of microbiological synthesis and order of procedure for treatment of culture fluid. In the following, we shall adhere to the same order in discussing the methods for isolation of microbial metabolites.

Little-described processes for producing concentrates are interesting. A particularly large number of problems arises because of the high hygroscopicity of most products in this group. They are produced most often in dry or liquid form for agriculture. In addition to special-purpose substances, they contain other metabolites, biomass of productive microorganisms, residues of nutrients and ancillary material (foam quenchers, agents for regulation of medium pH, etc.). The culture fluid is directly submitted to the simplest technology, i.e., concentration by removal of fluid; in other cases, some purification procedures or other are needed to remove part of the secondary components and, to some extent, increase the relative amount of special-purpose elements. As a rule, the concentrates contain a substantial share of product mass outside the cells of microorganisms, even if the specific [special purpose] substance is within the cell. This preparative form has the following advantages: simpler technology and, consequently, lower expenses for developing and implementing production; presence of additional components in concentrates; absence or smaller amount of industrial waste; with isolation of a crystalline product, the useful waste usually has the same technological properties as the concentrates.

Recovery of intracellular and extracellular metabolites in the form of pure substances is technologically very diverse and complex. Extraction of intracellular metabolites involves disintegration of cells. Most of the substances are thermolabile and have relatively large molecules. Much

theoretical and practical knowhow has been accumulated in the area of producing medical antibiotics [12]. As a rule, the first stage of the process consists of separation of mycelium from the liquid medium. Culture fluid is pretreated (acid and thermal coagulation, treatment with electrolytes, use of filtering powder, formation of fillers directly in fluid) in order to improve filterability and quality of filtrates, i.e., native solutions, and for subsequent successful isolation and chemical purification of products. The processes of isolation and chemical purification of antibiotics should yield products that are highly pure. In view of the fact that the concentration of antibiotics in unadulterated [native] solutions is quite low, and that there are numerous organic and inorganic impurities in solutions, the methods used for isolation and purification must be highly selective in capacity for significant concentration of end [special] products.

Extraction, ion exchange and precipitation are the most widely used methods for isolation and purification. The distinctive feature of all the methods is that there are many technological stages (repeated separation and filtration of precipitates, two- and three-step extraction, crystallization, concentration of solutions by vacuum evaporation, use of various drying methods, etc.), as well as diversity and complexity of equipment used, difference in size of the latter (at the first stages up to hundreds of cubic meters and at the last ones, occasionally several tens of liters). For example, use is made of the following: drum vacuum filters, press filters, pressure and suction [Nutsche] filters, separators and centrifuges varying in capability, various designs of extractors, ion-exchange columns, different systems of film evaporators, drying devices operating on the principle of diffusion, pseudoliquifaction, sublimation of ice and other types of equipment. In view of the fact that antibiotics are complex organic compounds, usually unstable and sensitive to the environment (high temperatures, change in pH of solutions, etc.), chemical purification processes must be conducted under conditions that provide for utmost stability of the products.

There are several specific sanitary requirements for the production of highly pure drugs, particularly those used by injection. The final stages (drying, packaging) should be conducted under aseptic conditions, for which not only special treatment of equipment, ancillary material, rooms and appropriate training of service personnel are required, but use of additional technological procedures, for example, purification of air going into the rooms.

Recovery of enzymes has been described extensively in the literature [13, 14].

In this survey, we have analyzed information and systematized the general methods for recovery of microbial metabolites in the form of concentrates and pure substances. Production of pure substances by enterprises under Glavmikrobioprom [Main Administration of the Microbiological Industry] is only at the development stage, whereas some knowhow has already been

accumulated by other agencies. Some experimental and practical work has already been done by the authors, which enables them to discuss the processes of isolation as they apply to amino acids, organic acids and certain enzymes.

Factors Affecting the Properties of Culture Fluid

There are diverse methods of preparing culture fluids, depending on the expected properties of the metabolite to be recovered. However, we can formulate some general principles of this technological stage:

1. The main fermentation should be run on clear [colorless] substrates that are as completely assimilable as possible, with the use of active strains. This provides for a minimal proportion of inert constituents to the specific metabolite being recovered in culture fluid and facilitates isolation of pure substances; it also increases the amount of end product in the concentrates. Thus, addition of acetic acid or saccharose to a molasses medium for recovery of lysine increases by 9% the productivity of ion-exchange equipment [15]. Use of acetic acid as the only source of carbon makes it possible to obtain concentrate with 50-72% lysine monochlorohydrate (15-20% on molasses media) or 97% pure crystalline lysine by means of direct desiccation of eluate on a spray dryer [16, 17]. Accordingly, the residual concentration of substrates and extraneous [secondary] metabolites must be reduced to a minimum. These substances worsen the physicomechanical properties of concentrates.

2. In most cases, the fermentation process must be intensive and well controlled in order to rule out the possibility of cell death at the stationary stage of growth. In addition to lowering the productivity of the culture, this worsens the rheological properties of culture fluids and makes subsequent treatment (filtration, centrifugation, etc.) difficult. There is little information in the literature concerning viscosity, surface tension and other physical properties of culture fluids. As an example, we can refer to the survey in [18].

3. Operational efficiency and quality of postfermentation operations to prevent access of extraneous microflora into culture fluid and reduce treatment time of the latter are particularly important. For example, the microbiological loss during production of feed lysine concentrate (KKL) could reach 66% of overall losses [19]. There is appreciable loss of glucoamylase after only a few hours of storage of culture fluid [20]. This is associated with the problem of stabilization of the metabolites being recovered. One must know the nature of product loss in order to select a stabilization method. In general, the losses consist of microbiological, chemical thermochemical and combined forms.

It is simplest to control microbiological loss (change in pH, antiseptic conditions, cooling, pasteurization and others), and in the other cases individual study of the process is necessary.

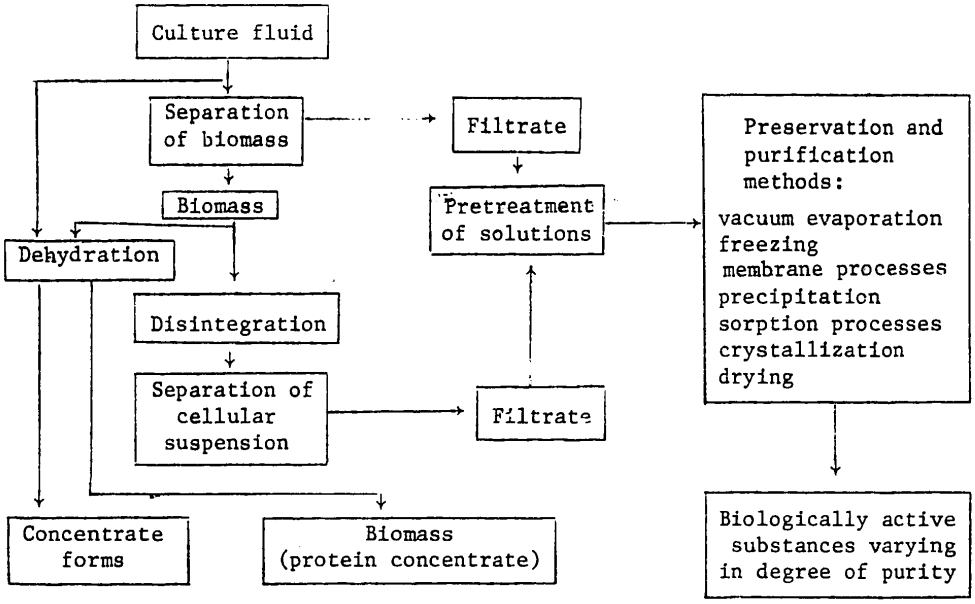

Figure 1. Diagram of recovery of products of microbiological synthesis

4. Standardizing the culture fluid for concentration of metabolite becomes a serious problem in producing concentrates, since the product to be recovered must be standard and have a specific composition. True, technologically this operation is simpler to perform with more concentrated intermediate products, for example, with evaporated culture fluid in the case of recovery of KKL.

Production of Concentrates

Microbiological concentrates of the end substance to be recovered can be divided into vitamin products--feed vitamin B_{12} concentrate [12], feed antibiotics--biomycin (biovit), "kormogrizin" and bacitracin; enzymes, amino acids and bacterials.

Among enzyme products, there is prevalence of the concentrate form, and only a few products produced on a large scale are submitted to utmost purification and crystallization. This is apparently attributable to the technical difficulty of purifying them and poor crystallizability. When recovering extracellular enzymes, in most cases the entire culture fluid is concentrated, or else, after removal of producer biomass, the

fluid is submitted to ultrafiltration, perhaps precipitation of enzymatically active protein and occasionally with additional purification. Extracted enzymes are also produced in concentrate form; the liquid form of enzyme products is widespread. Dry products are often found to be highly hygroscopic, and for this reason the product sticks to the surface of the dryer. To overcome the difficulties caused by these phenomena, an airtight container is used, filler is added before drying and, in particular, syrups are dried together with porous fillers.

Information about recovery of enzyme concentrates has been systematized rather well and summarized in monographs and analytical surveys (for example, [13, 14, 22, 23]).

With respect to amino acid production, lysine for feed purposes is produced on the largest scale. The original Soviet technology for production of KKL consists of recovering it in a sensible ["rational"] form, in the form of concentrates with high feed effectiveness that are produced using a relatively simple method [24-28].

Among the bacterials (agents to protect plants, bacterial fertilizers), there are both products consisting of cell biomass and those containing a significant amount of dry substances from culture fluid. The latter, i.e. extracellular concentrates, include, for example, antobacterin, insectin and others. Extensive studies of questions pertaining to drying bacterial products are being pursued at the Institute of Heat and Mass Transfer, Belorussian Academy of Sciences [18].

Amorphous structure is the typical property of concentrates [29]; it determines the absorptive nature of removal of moisture, high hygroscopicity, thermoplasticity and adhesiveness of the products [30, 31].

In most cases, the microbial concentrates do not meet the requirements, in their physicomechanical and technological properties, that would permit their direct use in the mixed feed industry and other branches of the national economy. This is feasible with the addition of fillers or preparation of premixtures by consumer enterprises [32].

Recovery of Feed Lysine Concentrate (KKL) from Culture Fluid

The concentration of dry substances in culture fluid constitutes 11-15%, including 2.8-4.3% L-lysine (monochlorohydrate), 1.6-2.2% bacterial biomass and 0.3-0.6% residual sugars.

During evaporation, after fermentation, the culture fluid is acidulated with hydrochloric acid to a pH of 5.5-6.0 and 0.17% sodium bisulfite is added to suppress development of extraneous microflora at different stages of treatment of this fluid and stabilization of lysine during heat treatment.

When there is incomplete assimilation of sugars by the main producer, after-fermentation is effected by means of adding a culture of Trichosporus cutaneum R-3 yeast.

The culture fluid is dehydrated in a vacuum evaporating device.

The most effective evaporation systems are those with a sinking film [?], for example the Vigant (GDR) brand equipment, which provides for minimal loss of lysine during evaporation.

The evaporated mass containing 35-40% dry substances is then passed into a spray dryer with disk sprayer [30] for further dehydration. Air, heated to 200-210°C at the inlet and 105-110°C at the outlet, is used as a drying agent. After drying, the product is cooled in a pneumatic conveyer [blower] and packaged in airtight containers. The KKL contains at least 15% L-lysine (monochlorohydrate) with no more than 10% moisture (first variant of prepared form, TU 59-72-74).

There are some difficulties involved in technology of spray drying of the evaporated culture fluid due to the hygroscopicity, thermosensitivity of active substances, and thermoplasticity of the product. To eliminate them, a method has been evolved for drying evaporated solution with addition of filler into the drying compartment of the unit [33]. The following powders have been tested as fillers: aerosil [silica] (GOST 14922-69), bone meal (OST NKPP 463), lime powder (MRTU 21-41-69) and defluorinated phosphate. In addition, pneumatic separating devices were installed instead of the mechanical gate valves ["sluice gates"].

To lower hygroscopicity of KKL, slaked lime is added to the evaporated culture fluid. The amount used depends on the required degree of reduction of hygroscopicity. At the Livany Experimental Biochemical Plant, 3-6% of the additive has been used since 1973, and this is sufficient for normal operation of the spray dryer. The amount of lime added is up to 20% (dry matter) at the plant in the city of Peshtera [illegible] (NRB), and this normalizes entirely the physicomechanical properties of KKL. At the Institute of Microbiology imeni A. Kirkhenshteyn, Latvian Academy of Sciences, studies conducted in 1968 revealed that upon contact of slaked lime with evaporated culture fluid there was formation of gel; a study was made of the optimum conditions for this process and spray drying of the gel.

The evaporated mass, with 45-60% concentration of dry substances and at least 7% L-lysine content, is passed into a reactor to obtain liquid [32, 34] KKL (second variant of prepared form, TU 88 Latvian SSR 04-74) or in order to dry it with filler on an apron dryer or fluidized-bed dryer.

In the third variant, the evaporated mass is mixed with filler--wheat bran (1:1 dry substance), and passed through a granulator to a dryer [35].

Drying time is 2-2.5 h at 90-95°C with the PKS-90 apron dryer and 20-25 min at 120-130°C with the fluidized-bed dryer designed by the Livany Experimental Biochemical Plant. A "vibrofluidized-bed" dryer is also being developed [36]. The obtained granules are ground and standardized with filler. The product, kormolysine RST BSSR 621-75, obtained by this method is not hygroscopic.

The loss of lysine with evaporation in the "sinking film" system does not exceed 3% [37]. The loss constitutes 5-7% in the spray dyer and 3-8% in the PKS-90 and fluidized-bed dryers. Total loss of L-lysine in the dehydration process ranges from 3 to 18%.

Metering devices and mixers are used to add vitamins [24] in order to make more economic use of KKL, and it is produced in the form of dry premixes (fourth variant of prepared form, TU 88, Latvian SSR 010-77).

Several hydrolysis plants produce lysine-enriched (at least 2%) yeast, in accordance with TU 59-84-75 [28].

In the course of assimilation of experimental industrial production of KKL, several technological refinements were developed and introduced [27], which pertain, in particular, to the prepared forms, methods and equipment for producing them [35, 36]. These methods, which improve the technology of production of KKL, can also be used in the production of other microbial concentrates. The evaporators and dryers used to obtain concentrates, and the dehydration modes were described in [18, 36-40].

Physicomechanical Properties of Concentrates, on the Example of KKL

Parameters and methods characterizing the suitability of concentrates for processing in the mixed feed industry and other consumer branches of industry have not yet been defined. Accordingly, the permissible ranges of parameters used in practice have not been set [41]. Vague descriptions are encountered, such as "bulk powder product," "nonhygroscopic product," etc. But most of the concentrates are amorphous substances [29], which can be referred to as highly concentrated aqueous solutions. Consequently, retention of fluid by means of absorption is inherent in the concentrates. The fluid is uniformly distributed in the product in an equilibrated state. The amorphic nature of the concentrates also causes a change in their mechanical properties, depending on the temperature.

It has been demonstrated that KKL conforms well with the law of Raoult, expressing equilibrium between voltaile component (water) content in the solution (concentrate) and pressure of vapor of the volatile component above the solution. In practice, this is manifested by hygroscopicity of the concentrates, i.e., a tendency toward more intensive absorption of fluid under natural conditions, with formation of lumps and a solid mass (with further absorption of moisture it changes into a viscous liquid).

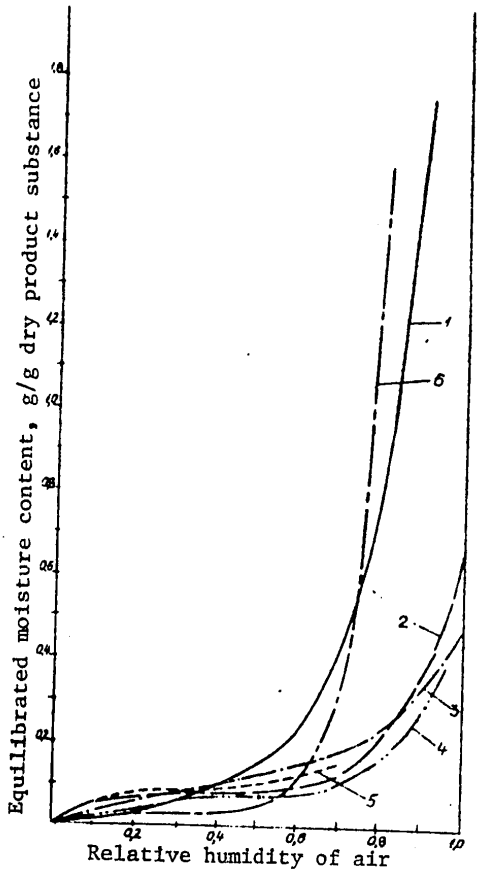

Figure 2.
Isotherms of moisture absorption by some microbial concentrates

1) feed lysine concentrate without filler, 25°C
2) vitobacterin, 20°C
3) kormogrizin, standardized, 20°C
4) biovit, 20°C
5) baker's yeast, 18°C
6) feed vitamin B_{12} concentrate, 25°C

Figure 2 shows the isotherms of absorption by some concentrates. Although the sorption isotherms are generally considered as the main characteristic of hygroscopicity, the rate of absorption, which determines changes in technical properties of concentrates, is an equally important indicator [42, 43].

Table 1 lists the relative atmospheric humidity, at which friability was impaired [35]. In this case, loss of friability was determined on the basis of behavior of a sample kept for 48 h in a weighing bottle in a desiccator (Ø 20 mm) at a specific relative atmospheric humidity (35.7, 43.1, 53.6, 61.8 and 85.1%). The size of the sample constituted 1.7 g. When friability was lost, the sample did not scatter [pour] when the bottle was rotated about its vertical axis.

Methods have been developed and systematized for reducing hygroscopicity of concentrates (Table 2) [42, 43]. In assessing them, special attention should be given to the results of zootechnical testing of the concentrates [26], since the use of fillers could have an adverse effect. The best indices were obtained with wheat bran in the production of KKL. This filler is particularly advantageous in the case of subsequent production of vitamin and amino acid premixes [24]. It is desirable to use up to 20% lime, in relation to dry substances, and this virtually normalizes the properties of KKL. The biological effectiveness and distinctions of giving animals such a product are being investigated.

Table 1. Characteristics of various commercial forms of KKL according to loss of friability

Method of recovery and drying KKL	Carrier	Carrier content in dry substance, %	L-lysine (monochlorohydrate) content, %	Relative humidity at which loss of friability occurs, %
Ordinary KKL, spray drying	-	-	18.5	35-40
Ordinary KKL, dry powder mixed with filler	-	85	2.6	53-60
Spray dyring of evaporated solution with yeast suspension (lysine-enriched yeast)	-	90	2.0	55-65
Apron dryer, fluidized-bed dryer for granules; vibro-fluidized=bed dryer	Bran, yeast (dry)	55	7.7	53-60
Fluidized-bed dryer with spraying of suspension	Yeast (dry)	55	7.7	53-60
Apron dryers, fluidized-bed (both types) and vibro-fluidized-bed dryers	Bran or dry yeast	70	5.2	70-80
Spray drying as suggested by ... [illegible]	Bran	50 65	8.6 6.0	40-45 53-60
Spray drying of evaporated solution with suspension of dry yeast	Yeast	60	6.9	45-55
Spray drying with addition of lime or other gel-forming	Lime	18-20	15	53-62
Mixed feed	-	-	--	>85

Table 2. Methods for reducing hygroscopicity of concentrates

Physicochemical	Technological	Factor determining suitability of the method, flaws	Example of use to process microbial and analogous products
Crystallization of product (or main mass)	Removal of impurities preventing crystallization	Concentration of end product and efficiency of removed components. The procedures (and equipment) are complicated and laborious; a large amount of liquid waste is formed	Known methods of purification of enzyme and other products by precipitation, ion-exchange resin, etc.
	Crystallization obtained by addition of primer. Crystalization by means of physical methods of treatment	Difficult to obtain crystallization of all components in the case of multicomponent products	Crystallization of lactose into milk powder
Reduction of amount of hygroscopic and vitrifying components	Removal of inert substances from main raw material	The process is relatively complicated and often not effective enough	Removal of salts from molasses by ion-exchange resin treatment
	Choice of components of nutrient medium, in particular, use of noninert hygroscopic components	Specifics of microbial culture	Use of saccharose or starch hydrolysates instead of molasses
	Incomplete removal of used vitrifying components (for example, sugars)	--	Use of organic acids as source of carbon [16, 17]

Physicochemical	Technological	Factor determining suitability of the method, flaws	Example of use to process microbial and analogous products
	Full use of components, i.e., salts in which both both cation and anion are used	--	Use of urea instead of ammonia salts as source of nitrogen
	Removal of hybroscopic components during or after fermentation:		
	by microbiological methods	Impossible to remove all hygroscopic factors	After-fermentation during recovery of KKL [44]
	chemical methods	Specifics of culture and end product (instability, etc.)	Not known
Structuring of liquid product (increasing viscosity, particularly of moistened product)	Creating gel structure. Sorption of product on sorbent	Use of large amounts of structuring additives, reduction of end product content. Not effective enough when moistened product is exposed to mechanical pressure	Use of lime and other gel-formng substances
Mixing with filler in powder form to retard moisture absorption and ... [illegible] of particles	Addition of fillers to product: hydrophilic (60-85%)	Reduction of end product content; filler efficiency not always obtained (with the exception of reducing hygroscopicity)	--
	hydrophobic (up to (30%)	--	Use of hydrophobized aerosil, calcium stearate

Physicochemical	Technological	Factor determining suitability of the method, flaws	Example of use to process microbial and analogous products
	ultrafine (up to 30%)	--	Use of aerosil as an additive to prevent caking [30]
Retarding moisture absorption on the basis of reducing specific surface	Granulation	Low effectiveness; the granules are not always acceptable for the conditions under which product is used	Well-known method of improving commercial properties
	Granulation with protective film, including microcapsuling	Combining permissibility and effectiveness of film material	Coating feed supplements with polyvinylchloride film
Chemical modification of product	Increasing molecular mass. Producing protective microgranules or other easily separating compounds	Conditions under which product is used, technical and economic considerations	Not known

There has been a study of the process of vitrification of amorphous microbiological concentrates in powder form; determination has been made of the temperature of this process and relation of thermal expansion of the specimen, in particular, KKL, amylosubtilin and yeast, to different levels of moisture content [30, 45].

Experimental data have been published on the physical properties of various commercial forms of KKL [46, 47].

Studies of the properties of concentrates make it possible to comprehend the causes and mechanism of formation of technical characteristics (specifications?] of products that are unsatisfactory for the consumer, and they also show the basic means of upgrading these characteristics. Zootechnical studies of various new commercial forms of concentrates and intermediate products of production thereof play an exceptionally important role, since use of additional substances or technological operations may yield an adverse biological effect in some cases. At the present time, there are no standard methods or criteria, according to which the suitability of concentrates for processing can be unequivocally determined. In the authors' opinion, the first and foremost task for the All-Union Scientific Research Institute of the Mixed Feed Industry to solve this problem, including coordination of research.
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MOLECULAR AND CELLULAR BIOPHYSICS

Moscow MOLEKULARNAYA I KLETOCHNAYA BIOFIZIKA (Molecular and Cellular Biophysics) in Russian 1977 pages unknown

/Annotation, Foreword, Introduction and Table of Contents of book. G.M. Frank, editor. Introduction by M.V. Vol'kenshteyn, Corresponding Member USSR Academy of Sciences/

/Text/ This collection consists of original studies conducted in 1971-1976 by associates of the USSR Academy of Sciences Institute of Biophysics. It contains papers concerning the most important results obtained in the areas of molecular biophysics and cellular biophysics. Problems discussed include problems of biological motility, conformational motility of macromolecules, electron-conformational concepts concerning the structure of biological macromolecules and modern methods of physico-chemical studies of biological structures and processes.

The collection is intended for a wide range of readers, including biophysicists, biochemists, specialists in molecular biology and cellular biology, graduate students and students specializing in the area of biophysics.

Foreword

The formation of a new science among the biological disciplines is always a complex, and in some respects, a contradictory process. This is the situation today in respect to biophysics. Skeptics sometimes question whether the formation of this new science is somewhat artificial or not. However, if we examine it attentively, we shall see that this process is a progressive step for biology as a whole and one which must continue.

The very same thing occurred several decades ago during the genesis of biochemistry. However, the establishment of biochemistry was facilitated by the evolution from physiology of "physiological chemistry," a term about which little is now remembered. However, it is easy to produce many demonstrations of the fact that "chemical language," even as complex

as it was, was still inadequate to describe even the individual links of the life processes. This produced the organic necessity for development of the physical examination of biological phenomena with all the powerful apparatus of modern physics, which includes both general theoretical concepts (especially mathematical apparatus) and modern methods of experimental physics.

First there arose the optimistic attitude which assumed that participation of physicists would lead to the rapid solution of biological problems. However, it soon became clear that pursuit of such an approach was impossible without some degree of simplification and schematization. Thus, investigators were once more convinced of the immense complexity of questions of biology.

Now we can be assured that the joint development of biochemistry and biophysics has contributed greatly to our understanding of the material essence of life phenomena.

We should not be disturbed by the fact that, evidently, biophysics does not have its own specific objectives or problems such as does, for example, microbiology or the science of photosynthesis, which limits its scope. This same biophysics is necessary for successful development of the two sciences mentioned above and, in dependence upon the posing of the problem, biophysical approaches are used in the solution of problems of microbiology and photosynthesis. Nevertheless we cannot exclude the fact (and really cannot even avoid it) that there will arise gradually (and already are arising) some problems in the solution of which biophysics prevails and in which the results of the research are decisive.

In view of this, we must not attempt to separate from biology individual problems in which biophysics operates "autocratically". The role of biophysics will be highly significant only when it is applied with reasonable interaction with biochemical and general biological approaches.

As the title indicates, this collection contains results of research concerning two major groups of studies conducted in recent years at the USSR Academy of Sciences Institute of Biophysics. They have been published in honor of this institute on its 25th anniversary.

The division of biophysics into molecular biophysics and cellular biophysics is somewhat arbitrary. It is difficult, today, to present concepts concerning the cell without inclusion of studies concerning biologically important associations, and, on the contrary, the study of the properties of biomacromolecules is conducted in consideration of their role in processes of the vital activities. Therefore, in spite of the

division of this collection into 2 sections, the reader will find many examples of overlapping of levels of the heirarchy of living matter.

The first section deals largely with the physical aspect of the structure and functional possibilities of macromolecules, which play a predominant role in biological systems. The major contribution of articles in this section is the formulation of new, theoretical concepts in the area of the kinetics of biomolecular processes in quantum chemistry. At the same time, we must point out that many of the theoretical conclusions are illustrated by impressive experimental confirmations.

Studies in the area of biological motility and muscle contraction are presented in the 2d section. The arbitrariness mentioned above of the separation of the molecular and cellular levels becomes more obvious here. Today, for example, we cannot speak of the mechanism of muscle contraction while examining only the transverso-striated structure of the muscle without considering, at the same time, the behavior of muscle proteins, localized in individual parts of the muscle fiber.

On the whole, the collection confirms the statement above concerning the inseparableness of biophysical studies from biochemical approaches or, in general form, from the physico-chemical concepts concerning the properties of living structures.

The USSR Academy of Sciences Institute of Biophysics, upon its 25th anniversary, is utilizing the possibilities of theoretical and experimental physics in the development of present day concepts of biophysics so that it continues to occupy a place of honor in some other biological disciplines.

Introduction

Molecular biophysics involves, primarily, a study of the structure and properties of biopolymers -- proteins and nucleic acids. This scientific trend has developed over the last 2-3 decades to a greater extent than other areas of biophysics primarily due to the rapid progress in molecular biology and biochemistry and by the elucidation of the molecular bases of the most important phenomena of vital activity, such as heredity, variability, metabolism, and specific enzymic processes.

Research in the area of the physics of macromolecules underway at the USSR Academy of Sciences Institute of Biophysics includes studies of both globular and fibrillar proteins. The first area refers to different enzymes and hem-proteins devoid of enzymic activity (myoglobin and hemoglobin) and also receptor proteins (rhodopsin and others). Fibrillar proteins include, primarily, contractile proteins of the muscles such as

actin, myosin, tropomiosin and also collagen. All of these objects may be considered to be key products for one or another of the biological processes.

The study of proteins is not an end in itself. There is an ever increasing number of molecular-physical studies involving the most important problems of the biophysics of cells -- membrane transport in connection with light and molecular receptions and muscle contraction.

Such molecular-physical studies properly involve an experimental and theoretical study of enzymic processes, the study of the behavior of proteins in solutions (an actomycin complex) and the development of original methods of research (especially, acoustical research).

Studies being conducted in the area of the physics of nucleic acids include studies of the structure and properties of DNA, RNA, model synthetic polynucleotides in connection with processes of replication and transcription in connection with problems of stabilization of these biopolymers.

A significant part of the research concerning molecular biophysics is combined with general theoretical concepts of electron-conformational interactions (EKV). The function of biopolymers is chemical and electronic. They function either as converters of chemical, molecular signals (enzymes and other proteins) or as chemical matrices in protein biosynthesis (DNA mRNA). This function is realized by means of conformational changes of biopolymers. The problem consists of the study of the interaction of electron and conformational degrees of freedom.

The concept of EKV was formulated for the first time at the institute. The solution of pertinent problems requires a wide range arsenal of modern experimental methods and theoretical studies also in the area of quantum chemistry. Effective use is made of diverse optical and spectral methods, especially the technique of pulse photolysis and also of the study of electron paramagnetic resonance (EPR) spectra of spin labeled biopolymers.

Enzyme-proteins may be treated as the "black box" which realizes transformation of the input molecular signal, the substrate, into the outgoing signal, the product. The study of the structure and the operation of such a "black box" is performed by two methods: by the study of the conversion process, that is, the kinetics of the enzymic reactions, and by the study of the structure and dynamics of the converter itself. This section presents results obtained by both methods. Reactions of regulator enzymic systems are studied experimentally and the role of comparatively slow conformational conversions of proteins are revealed. The properties and mechanisms of action of RNA-polymerase are studied alongside enzymes of

dehydrogenase type with hem-containing proteins. A theory of the kinetics of enzymic reactions based on methods of the theory of graphs is constructed. These methods developed at the institute give the simplest algorithms for calculation of the rate of the reactions. At the same time, model quanto-chemical calculations which permit an understanding of the nature of EKV in enzymes and in non-enzymic hem-containing proteins are undertaken. The processes of electron transfer in hem-containing proteins, directly associated with EKV, are studied experimentally. An original arrangement for the study of photoconversions of proteins by a pulsed photolysis method is constructed. This provided new information concerning the properties of hem-containing proteins and rhodopsin -- the protein responsible for visual reception.

The important theoretical method of atoms -- atoms of potentials is used for analysis on nonvalent interactions and for the study of conformational transitions of polynucleotides, for the study of solvation of organic molecules and prediction of the structure of crystals of model compounds. The structure and properties of protein crystals are studied with the help of X-ray methods and other methods.

Original concepts concerning the liquid-crystalline structure of contractile proteins provide the basis for some studies devoted to consideration of muscle contraction. Many studies now involve the liquid crystalline structure of membranes, which determine conformational properties of lipids.

However, the idea concerning the liquid crystalline structure of protein contractile systems, developed for the first time at the institute, is of a different nature. Liquid crystalline properties of contractile proteins are determined not by the conformational motility of proteins nor by the packing of their sub-units in the fibrilla but by the behavior of the fibrillar proteins as integral systems.

It is quite necessary to mention the development of high speed X-ray diffractometry of proteins, an original X-ray method based on the use of synchrotron radiation.

In studies devoted to the photochemistry of the visual pigment, roentgenography of muscles, the structure of collagen, the peculiarities of behavior of proteins of the actomycin complex in solution, the "bridges are being built" between molecular biophysics and the biophysics of cells. Such a division of biophysics is, of course, somewhat arbitrary. It has an historical nature and there are no rigid boundaries here. The general problem involves the study of biological phenomena at the molecular level.

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BACTERIORHODOPSIN AND THE VISUAL PIGMENT RHODOPSIN: AS DISCUSSED AT SOVIET-AMERICAN SYMPOSIA

Moscow VESTNIK AKADEMII NAUK SSSR in Russian No 9, 1979 pp 120-127

[Article by M. A. Ostrovskiy, Doctor of Biological Sciences]

[Text] Several Soviet-American symposia were held in recent years on "New Directions in Biology." The first symposium, held in Kiev in 1975, was devoted to nucleic acids, the second in Chicago in 1976 dealt with research on biological membranes, the third in Riga in 1976 was concerned with protein chemistry and physics, and the latest, held in Kiev in October 1978, again dealt with biological membranes. The Soviet chairman of the organizing committee was Academician Yu. A. Ovchinnikov, vice president of the USSR Academy of Sciences.

A great deal of attention was paid at the somposia to the structure and function of biological membranes and membrane proteins.

The molecular and membrane mechanisms of nerve excitation was extensively discussed at the last Kiev symposium. The principal subject was the structure and function of ionic channels of excitable membranes.

Important information is now available on the electrical and chemical processes responsible for the origination and propagation of nerve signals. It is a well-established fact that the ionic currents in the excitable membranes of nerve cells are created by discrete molecular complexes, the so-called ionic channels. Facts are being rapidly collected on the properties of specific ionic channels. The identification and investigation of their functional properties in model systems is on the agenda. In the Soviet Union, this research is being conducted on the highest level, particularly in Kiev by Academician P. G. Kostyuk and his students (Institute of Physiology imeni A. A. Bogomolets, Ukrainian Academy of Sciences). Hence Kiev has quite rightly become the place for holding a Soviet-American symposium on biological membranes.

The paper of P. G. Kostyuk "Calcium Conductivity of the Nerve Cell Membrane" and that of his student O. A. Kryshtal' "Study of the Conductivity and Kinetics of Solitary Calcium Channels" examined the electrical and kinetic

characteristics of calcium channels. Soviet and American scientists discussed in detail the functional properties of channels specific for other physiologically important ions, chiefly sodium and potassium. Mention must be made in this connection of C. Armstrong's (USA) paper "Inactivation of Sodium Conductivity and Portal Currents," B. Hille's (USA) paper "Selectivity and Flow in the Ionic Channels of Excitable Cells," S. Hagivar's (USA) paper "Properties of the Potassium Channel of Anomalous Rectification," and B. I. Khodorov's (Soviet Union) paper "Inactivation of the Sodium Portal Current." The studies on chemically regulated (e.g., cholinoreceptor) and electrically excitable membranes are of extreme theoretical and practical interest, especially for present-day neuropharmacology, psychopharmacology, surgery, etc.

A subject of major interest at the symposiums was the structure and function of the visual pigment rhodopsin and bacteriorhodopsin. In the Soviet Union, research in this field is being actively conducted as part of the Rhodopsin Project directed by Academician Yu. A. Ovchinnikov.

Rhodopsin and bacteriorhodopsin have now become a "burning issue" in physicochemical biology. Bacteriorhodopsin is a concern of bioenergetics while rhodopsin is involved in sensory reception and nerve excitation. Bacteriorhodopsin is responsible for the simplest and probably the most ancient (nonchlorophyll) form of photosynthesis while rhodopsin is responsible for transforming the energy of light into visual (nerve) excitation.

A visual pigment, later called rhodopsin, was discovered more than one hundred years ago (in 1876) by the German physiologist F. Bolle. Bacteriorhodopsin was found in the purple membranes of halophilic bacteria by W. Stokkenius (USA) as recently as 1971. And, paradoxical as it may seem, we now know much more about the structure and function of bacteriorhodopsin than we do about rhodopsin. The purple membrane of halophilic bacteria proved to be a new type of biological membrane capable of transforming solar energy. It is part of the cell membrane of the bacterium Halobacterium halobium and it contains a single protein. This protein uses the energy of light to transport protons across the membrane. As a result, considerable electrochemical potential is generated on the membrane. The cell utilizes this energy to synthesize ATP and perform some other physiological functions. The bioenergetic (photosynthetic) function of bacteriorhodopsin is directly related to the photochemical cycle of transformation.

The visual pigment rhodopsin is also essentially a solitary protein in the photoreceptor membrane of the visual cell of the retina (it accounts for approximately 90% of the entire membrane protein). A direct relationship was detected long ago, and is by now firmly established between the phototransformations of rhodopsin and vision. The photochemistry and biochemistry of rhodopsin have been fairly well studied, but the mechanism responsible for coordinating the photolysis of rhodopsin and the generation of photoreceptor potential (visual signal) is still obscure.

What is the basis for calling the protein of purple membranes bacteriorhodopsin by analogy with rhodopsin? The similarity is quite great. Both are chromoproteins, typical membrane hydrophobic proteins, and both contain retinal (vitamin A aldehyde). Retinal is bound in both rhodopsin and bacteriorhodopsin to the amino group of the lysine radical of opsin. Retinal by itself is almost colorless, but in rhodopsin its maximum absorption spectrum strongly shifts to the red region, to 500 nm, while in bacteriorhodopsin it does so even more strongly, to 570 nm. The nature of this enormous bathochrome shift has still not been definitively elucidated. It is generally known that a large part of the shift in both rhodopsins is due to the protonizing of the bond between the aldehyde group of retinal (CHO) and the amino group ($E\text{-}NH_2$) of lysine. The molecule of retinal, since it is a polyene, can occur in several isomeric configurations. It was shown in J. Wald's laboratory at the end of the 1950's that of all the possible isomers, only 11-cis retinal can act as a chromophore of every one of the visual pigments and that the only photochemical reaction in the visual process is the photoisomerization of retinal from 11-cis to the all-trans form. So too in the bacteriorhodopsin molecule: Only certain retinal isomers (the all-trans and 13-cis forms) can function as its chromophore group. Some reports have been published on 11-cis retinal occurring in bacteriorhodopsin, but they are incorrect.

That the photoisomerization of 11-cis retinal performs a trigger function in the mechanism of visual reception is beyond doubt. As for the possible function of the isomerization of retinal in the bacteriorhodopsin molecule, there is still no reliable evidence that this reaction is involved in the performance of its main function, i.e., proton translocation across the purple membrane.

At the Biophysics Congress held in Copenhagen in 1975, R. Henderson (Britain) demonstrated (not on the program of the congress) a tridimensional model of the organization of the bacteriorhodopsin molecule in a membrane. According to this model, which is based on an electron-microscopic picture with a resolution of 7 Å, the molecule consists of seven alpha-spiral fragments that intersect the purple membrane at an almost 90° angle. In other words, bacteriorhodopsin is a transmembrane protein.

The methods of protein chemistry used for water-soluble proteins are well established, but they are scarcely suitable for hydrophobic membrane proteins. More effort should be made to develop new techniques for investigating these proteins, chiefly bacteriorhodopsin.

A successful method for splitting the bacteriorhodopsin molecule directly in the purple membrane was devised in the laboratory of Academician Yu. A. Ovchinnikov (Institute of Bio-Organic Chemistry imeni M. M. Shemyakin, USSR Academy of Sciences). The proteolytic enzyme papain became the instrument. Papain attacked fractures of the semifragmented molecule emerging on the

hydryophilic surface of the purple membrane. It is interesting to note that the investigators of bacteriorhodopsin traveled here over the path already marked for rhodopsin.

Academician Yu. A. Ovchinnikov in a paper on "Structure of Bacteriorhodopsin in the Light of Its Function" read at the Kiev Symposium set forth the complete amino acid sequence of the first membrane protein, bacteriorhodopsin (its molecule consists of 247 amino acid radicals and its molecular weight is 26534).

The relationship between the structure and function of bacteriorhodopsin is of particular interest. In this connection it is exceptionally important to know not only the amino acid sequence (primary structure) of the membrane protein but its topography in the purple membrane. The absorption of light by retinal is the primary event in the chain of molecular processes responsible for proton translocation. According to the data obtained in Ovchinnikov's laboratory, the aldimine group that binds the retinal (chromophore) radical to lysine-41 of the protein part of the molecule is 15 to 17 Å away from the side of the purple membrane onto which the N-end of the polypeptide chain exits. Since the first and rapid phase of proton transport across the membrane is associated with its emergence from the membrane into the environment while the second and slower phase is associated with protein absorption from the internal cytoplasmatic side of the purple membrane, Ovchinnikov and coworkers are right in assuming that the site where retinal combines with opsin (the protein part of the molecule) is close to the external side of the membrane.

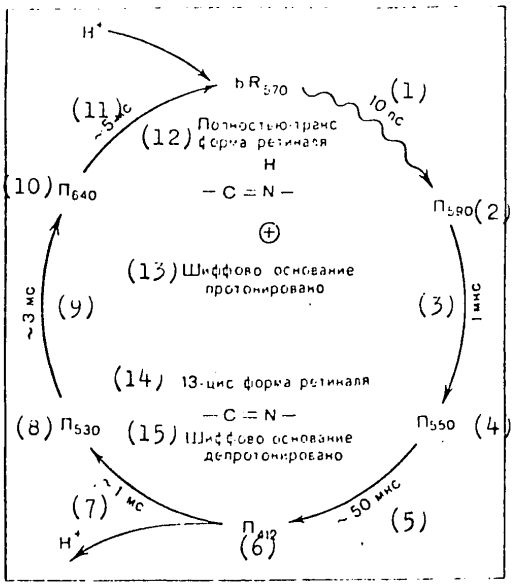
This work on interpreting the complete primary structure of the membrane protein of bacteriorhodopsin is exceptionally important. It opens up realistic prospects for determining the primary structure of rhodopsin and other proteins.

Let us now examine in some detail the function of bacteriorhodopsin, the main subject of the papers read at the Soviet-American symposiums by Professor Stokkenius and V. P. Skulachev, corresponding member of the USSR Academy of Sciences.

In a paper entitled "Outlook for Bio-Organic Chemistry and Molecular Biology" that Stokkenius read at an international symposium in Tashkent in October 1978 and before that at a Riga symposium in August 1976, he discussed at length the reactions of the photochemical cycle of bacteriorhodopsin. He showed that the duration of the photoreaction cycle is several milliseconds. In the course of the cycle one proton is freed on the external side of the membrane while another is bound on its internal side.

The initial rapid photochemical reactions were subsequently investigated by means of picosecond laser spectroscopy. Upon the absorption of light, bacteriorhodopsin changes into the so-called batho-form in a few picoseconds.

At the symposium in Tashkent, Stokkenius demonstrated the photoreaction of the bacteriorhodopsin cycle. The lifetime (half-life) of each of the intermediate products is given for a suspension of isolated purple membranes in water at room temperature and neutral pH. All-trans and 13-cis are the isomeric forms of retinal that were extracted under conditions in which a large part of the pigment is in the form of the original retinal and intermediate product P_{412}. The absorption and liberation of the proton is shown here in accordance with changes in the pH in the aqueous phase.



Photochemical cycle of the transformation of bacteriorhodopsin (according to W. Stokkenius)

bR_{570} - bacteriorhodopsin; P_{590}, P_{412}, P_{530}, P_{640}

Key:

1. 10 picoseconds
2. P_{590}
3. 1 microsecond
4. P_{550}
5. ~50 microseconds
6. P_{412}
7. ~1 millisecond
8. P_{530}
9. ~3 milliseconds
10. P_{640}

11. 5 milliseconds
12. All-trans form of retinal
13. Schiff's base protonized
14. 13-cis form of retinal
15. Schiff's base deprotonized

The kinetic parameters of this reaction cycle were recently analyzed in detail by Stokkenius aided by a special computer program.

To understand the molecular mechanism of proton transfer, it is necessary to determine the structure of the various spectrally distinguishable intermediate products. The technique of resonance Raman spectroscopy was successfully used for this purpose. Lewis, Stokkenius and their co-workers showed that in the original bacterorhodopsin 570 the binding of Schiff's base between retinal and the protein (opsin) is protonized but in the intermediate product P_{412} it is not protonized. This means that Schiff's base in the bacteriorhodopsin molecule is a very likely participant in the process of proton translocation. Lewis' very recently published data indicate that deprotonization occurs in the stage where the product P_{550} is converted to the product P_{412}.

The kinetics of proteon liberation and absorption in the aqueous phase on both sides of the membrane was recently investigated in detail in Stokkenius' laboratory. Using the technique of flash photolysis and pH indicator stains, Stokkenius found that proton liberation recedes its absorption and that one proton is liberated for each molecule of bacteriorhodopsin that passed through a conversion cycle. The H^+ yield largely coincides with the rate of accumulation of the product P_{412} while absorption is consistent with the regeneration of bacteriorhodopsin 570.

In one of their early studies, Osterheld and Stokkenius (1973) pointed out that the main function of bacteriorhodopsin is light-dependent proton translocation. This function was clearly demonstrated in models containing bacteriorhodopsin and lipids. Essentially two kinds of models were used: (i) a suspension of small vehicles usually about 100 Å in diameter or somewhat larger and (ii) flat lipid membranes (films) about a lipid bilayer. As Stokkenius noted, these models were used most successfully to investigate purple membranes in the laboratory of V. P. Skulachev, corresponding member of the USSR Academy of Sciences, at Moscow University.

At the Kiev symposium Skulachev presented new data on the temporal characteristics of bacteriorhodopsin as a molecular generator of electric current. A method was devised in his laboratory for direct recording of the difference in electric potentials generated by bacteriorhodopsin. The method involves incorporating fragments of purple membranes into a flat lipid membrane and then measuring the transmembrane difference in potentials by the ordinary electrometric technique. The method was significantly modified by replacing the artificial lipid membrane with porous carriers (membrane filters or collodion films) saturated with a solution of phospholipids, thereby substantially increasing the stability of the membranes.

Several phases of the electric response to a laser flash (at a wavelength of 530 nm and flash duration of 15 nsec) were observed in these experiments. The authors attempted to relate each of the phases to the formation of a particular intermediate product in the photochemical cycle of bacteriorhodopsin. They related the first (nanosecond) phase of generation of membrane potential to the first stage of the photochemical cycle, the second (millisecond) stage to ejection of the proton into the environment, and the third (millisecond) stage to proton translocation from the opposite side of the membrane (cf. the diagram).

Thus, a qualitative correlation was noted between the phases of generation of membrane potential and the spectral transformations of bacteriorhodopsin.

While the function of the bacteriorhodopsin molecule is now solidly established, that of rhodopsin is still largely obscure. Rhodopsin is a constituent of the photoreceptor membrane. In mammalian rods and cones these membranes form numerous flat disks or saccules. After a quantum of light is absorbed by the rhodopsin molecule in the photoreceptor membrane of the disk, electric potential (photoreceptor signal) arises on the plasma membrane of the visual cell.

An entire chain of processes occurring at the molecular, membrane, and cellular levels of organization must exist between the primary photochemical events in the disk and the secondary events on the cell membrane.

In a paper presented at the Kiev symposium, we distinguished at least two points, two mechanisms of coordination of the absorption of light by rhodopsin and the appearance of a photoreceptor (visual) signal. The first is that between the photoactive (photolysis) rhodopsin molecule and the functional (enzymic, ionic) changes in the photoreceptor membrane of the disk. The second is that between the light-induced processes in the disk and the blocking of the sodium channels in the plasma membrane of the rods and cones. It is the blocking of these channels that provokes a hyperpolarization reaction in the cells in response to light, i.e., to the origination of photoreceptor potential or visual signal in the rods and cones of the mammalian retina.

The key role in the mechanism of the "second" coordination--between the disk and the cell membrane--is played by calcium ions and cyclic nucleotides, specifically, cyclic guanosine monophosphate. J. Brown (New York University) presented at the Chicago symposium the results of direct electrophysiological experiments in which an increase in the calcium concentration within a rod in darkness results in hyperpolarization of the cell membrane, thereby simulating the action of light, whereas a decrease in the free calcium concentration results in depolarization of the cell, thereby simualting darkness. This means that calcium is in fact able to function as an intracellular mediator between the disk and the cell membrane. However, it still remains to be proven that under natural conditions in a native visual cell

light actually causes the free calcium concentration to increase within the cytoplasm of a visual cell.

The fact that the photoreceptor membrane of a rod disk becomes more permeable to calcium ions in the presence of light was reported by M. Ostrovskiy in Chicago and by W. Hubbell (University of California, Berkeley) in Riga.

The experiments involved essentially the following. Isolated photoreceptor disks or artificial liposomes modified by rhodopsin were "loaded" with calcium in darkness. The escape of calcium ions from the disks or liposomes into the incubation medium was then recorded in the presence of light by three independent methods.

It followed from the experiments performed in Berkeley and in Moscow that the ionic permeability of a photoreceptor membrane increases as a result of the photolysis of rhodopsin. However, it is still an open question whether calcium escapes from the disks in native visual cells and does so in an adequate amount. According to recent data obtained in our laboratory, calcium does escape from native disks, but it is unclear whether the amount is sufficient to ensure the formation of a visual signal.

Thus, it is likely that calcium plays a role in the mechanism of the "second" coordination, i.e., in the mechanism of intracellular transmission of a visual signal from a photoreceptor disk to the cell membrane, but there is as yet no conclusive proof of this. Besides calcium, the nucleotide cyclic guanosine is another very important factor in the process.

The mechanism of the "first" intramembrane coordination is not too clear. How does the ionic permeability of the photoreceptor membrane increase as a result of the photolysis of rhodopsin? How is the phosphodiesterase bound to this membrane activated (the concentration of cyclic guanosine monophosphate in a visual cell decreases as a result of the photoactivation of this enzyme)? How are other ionic and enzymic processes regulated here? Change in the electric properties of the photoreceptor membrane might well play an important role in the "first, intramembrane mechanism of coordination.

We cannot at present use the ordinary microelectronic technique to investigate the electric parameters and photoelectric reactions of the photoreceptor membrane of a disk because the size of a native disk is too small. Hence other approaches are needed.

M. Montal (University of California, San Diego) and M. A. Ostrovskiy also read papers at the last Kiev symposium on the photoelectric reactions of a photoreceptor membrane.

Montal was able to simulate a membrane system by incorporating rhodopsin into a lipid monolayer. This asymmetrically oriented rhodopsin-lipid monolayer was placed on a very thin Teflon film separating the two aqueous phases. A light flash elicited a rapid photoelectric response which, according to Montal, resulted from the division of electric charges in the oriented rhodopsin molecules. Montal also reported change in the ionic permeability of a photoreceptor membrane in the presence of light and, a matter of especial interest, the existence on it of potential-dependent ionic channels.

Thus, judging by these data, the electric properties of an artificial lipid membrane modified by rhodopsin clearly change.

V. I. Bol'shakov, G. R. Kalamkarov, and the writer using two different methods were able to observe photopotential of about 10 mv arising on the photoreceptor membrane of a disk. In the first series of experiments, we used the method of penetrating ions (anions) suggested 10 years ago by Ye. A. Liberman and L. M. Tsofina to detect and investigate potentials arising on different conjugating membranes of mitochondria and bacteria, including the purple membranes of Halobacterium halobium. When suspensions of closed disks were exposed to light, the anion concentration in the incubation medium decreased because the anions were absorbed by the photoreceptor disks. This meants that the absorption of light by rhodopsin on the photoreceptor membrane gave rise to electric potential with a "plus" sign on the internal surface of the disk. The anions entered the disk electrophoretically via the electric field.

However, the method of penetrating ions has definite limitations. An attempt was therefore made to measure electric potential directly on the photoreceptor disk using the ordinary electrometric technique. We adopted for this purpose the method of L. A. Drachev and V. P. Skulachev that enabled them to record the different phases of photopotential on the bacteriorhodopsin purple membrane. The photoreceptor disks "stuck" quite tightly to the flat lipid membrane (porous filters saturated with a solution of phospholipids were used). Switching on visible light resulted in the generation of substantial photopotential, about 10 to 15 mv, on the flat membrane. According to the Drachev-Skulachev electric circuit, the sign of potential was the same as in the experiments with penetrating ions, "plus" on the internal surface of the disk membrane.

Thus, substantial light-induced potential could be recorded on a photoreceptor disk by two independent methods. It was the direct result of the photolysis of rhodopsin.

It is quite possible that photopotential plays an important role in the mechanism of the "first" coordination--between the pholysis of rhodopsin and the secondary ionic or enzymic processes in a photoreceptor disk. If the potential on the purple membrane generated by bacteriorhodopsin is included in the chain of bionenergetic processes, it may also be included on the photoreceptor membrane in the chain of information processes.

There is still another important difference, in our opinion, between bacteriorhodopsin and the visual protein rhodopsin: The former apparently performs only one function, i.e., the function of consuming the energy of light from a proton pump. The latter, on the basis of all the evidence, is polyfunctional, for it triggers and regulates several light-dependent reactions in the photoreceptor membrane of a disk. However, the functional significance of these reactions for the formation of a fairly rapid (milliseconds) photoreceptor signal or for the realization of a fairly slow (minutes) process of light and dark adaptation is still obscure.

The Soviet-American symposiums clearly showed that both rhopsin and bacteriorhodopsin are now the focus of physicochemical biology, notably, membranology, bionergetics, and receptor.

Research on bacteriorhodopsin is opening up new prospects for using solar energy. Studies on visual reception are very important for medicine (to help understand the causes of serious diseases of the retina and work out new therapeutic approaches), chemistry, and engineering bionics.

5214
CSO: 1840

II. ADVANCED MEDICAL TECHNOLOGY

STANDARDS REGULATING THE PHARMACEUTICAL SERVICE

Moscow SBORNIK NORMATIVNYKH AKTOV PO APTECHNOY SLUZHBE (Collection of Standards Regulating the Pharmaceutical Service) in Russian 1979 signed to press 3 May 79 pp 2, 3, 647-656

[Annotation, Foreword, and Table of Contents from book edited by M. A. Klyuyev , Izdatel'stvo "Meditsina", 55,000 copies, 656 pages]

[Text] Annotation

Official legislative documents concerning the organization of the pharmaceutical service in the USSR are published in this collection. This publication includes the principal decrees, orders, and instruction regulating the work of institutions in the pharmaceutical network and the labor of pharmaceutical workers--documents required for organizational purposes by pharmacy directors, pharmaceutical warehouses, pharmaceutical factories (production operations), control and analysis laboratories, and other pharmaceutical institutions. Documents effective as of 1 April 1979 are encompassed.

Foreword

The present stage of development of the socialist economy and growth in the scale of social production are imposing new, higher requirements on legal regulation of economic activities.

Economic legislation must promote further growth of social production, and it must raise its effectiveness in the tasks of communist development. It must insure efficient operation of all elements of the economic mechanism, attainment of a correct relationship between the rights and responsibilities of all levels of the national economy's control, promote all-out development of the initiative of the ministries and departments, as well as of associations, enterprises, and other economic organizations, and encourage expansion of khozraschet relationships, growth in the role of business contracts, and further reinforcement of socialist legality and state discipline.

This collection is one of systematized official regulations on the main problems of the organizational, pharmaceutical, and business activities of pharmaceutical institutions in the USSR, regulations that are binding upon workers in all pharmaceutical institutions irrespective of their departmental subordination.

The regulations presented here are those effective as of 1 April 1979.

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UDC 002.6

FRAGMENT INFORMATION SUBSYSTEM IN PHYSIOLOGY AND MEDICINE

Moscow VESTNIK AKADEMII NAUK SSSR in Russian No 10, 1979 pp 52-54

/Article by Candidate of Pedagogical Sciences D. I. Blyumenau, Candidate of Medical Sciences K. F. Britikova, and Candidate of Biological Sciences S. I. Nudman and I. V. Sorokina/

/Text/ The steady increase in the role of scientific information connected with the progress of science and technology requires a search for more refined forms of providing scientific research with information. Integral information systems, by means of which a combination of such services as a selective dissemination of information, reference service, preparation of abstract and bibliographic publications, circulation of local information retrieval systems and so forth is performed, appear as some of the means creating the possibility of raising the level of software.

The idea of a one-time input of information (one-time processing of input documents), which forms the basis for integral information systems, has gained wide recognition among specialists in information services and its development is continuing. The overwhelming number of currently operating integral information systems function primarily as documentary service systems, that is, they ensure in a certain mode the issue in the final analysis of primary documents to the consumer, who has to extract the necessary information from them by himself. The importance of the development of such systems for improving the efficiency and quality of service for large groups of specialists is indisputable. However, they do not fully solve one of the most serious problems of information service--the issue of relevant information, that is, corresponding to the consumer's needs in a volume in which an individual specialist can assimilate it.

The study performed by the authors of this article at the Institute of Physiology imeni I. P. Pavlov of the USSR Academy of Sciences was based on the hypothesis on the possibility for such a form of information service in which a certain spectrum of standard information needs of certain groups and categories of specialists would be met not by the full text of the primary source, but by its standard fragments with an independent information meaning outside the document context. The array of such standard fragments

singled out at the stage of one-time input of documents into integral information systems through their formal and meaningful analysis should form an independent subsystem, which we call the Fragment subsystem. The development of such a subsystem should eliminate in large measure the negative aspects of the excess of documentary flow.

A standard independent fragment of a text implies a meaningfully closed context of a document, in a particular case in the form of a table, diagram, formula and so forth, understood outside the text of the entire document and capable of meeting, without turning to the primary source as a whole, the standard information need, that is, the need characteristic of certain stages in the creative activity of certain categories and groups of specialists in certain fields of knowledge. For example, S. L. Kruglov believes that standard needs are dictated by the conditions of a specific problem. It can be assumed that in primary documents a certain set of standard information needs connected with the performance of certain standard tasks can be met by certain types of text fragments sufficiently informative and independent to satisfy these needs. In this case the system in answer to a need standard in form should issue, for example, not a certain number of documents, in which the availability of relevant information is still hypothetical, but directly the text fragments containing relevant information.

Postulating the hypothesis on the possibility of a formalized extraction from documents of fragments of independent importance, we assume a priori that such fragments cannot meet all the needs, even standard needs. Therefore, in many cases an entire document will be necessary and in others, the level of a fragment's conversion, that is, of its information content, can prove to be unacceptable. Therefore, the main object of the studies discussed was limited to the clarification of the fundamental possibility for the establishment of similar types of integral information systems for physiological and medical subjects.

When the problem of the independent importance of a certain fragment was solved, two conditions were laid down: a) the text had to be comprehensible without the use of information from the other parts of the document (with the exception of the title; every fragment is accompanied by a bibliographic description of the article); b) the text should correspond to the standard information need. The degree of independence of the singled out fragments was evaluated by four experts--specialists in the field of physiology and medicine.

The experiment was conducted on two files of documents. The content of 220 articles published in FIZIOLOGICHESKIY ZHURNAL SSSR imeni I. M. Sechenov in 1978 and 60 articles from the journal NEYROFIZIOLOGIYA of the same year were studied initially (survey articles were not used, because in their structure they did not lend themselves to fragmenting corresponding to the task set). An examination of the structure of articles published in these journals showed its identity. In particular, in these articles it is

possible to single out fragments for such subjects as the "state of the problem," "method of research," "research results" and "discussion of the results obtained." It is very important that, basically, these fragments are noted in articles by the appropriate titles and singling them out does not present special difficulties. As a result of the work on fragmenting articles from both journals, we obtained the data presented in the following table.

Results of Fragmenting Articles From Physiological Journals

Name of journal	Number of scanned articles	Number of Singled Out Fragments (Aspects)			
		"State of the problem"	"Method"	"Results"	"Discussion"
FIZIOLOGICHESKIY ZHURNAL SSSR	220	220	220	148	148
NEYROFIZIOLOGIYA	60	60	60	50	50

As can be seen from the table, individual fragments the "state of the problem" and "method of research" were singled out in all the 220 articles of FIZIOLOGICHESKIY ZHURNAL SSSR, but the fragments "results" and "discussion" could be singled out only in 148 articles, because in 72 articles these sections were organically interconnected and were read as a single whole (the subtitles in these articles were called "results of experiments and their discussion"). Thus, of the 220 articles studied in this journal 736 individual fragments were singled out. In the journal NEYROFIZIOLOGIYA in 10 articles the sections "research results" and "discussion" did not lend themselves to fragmenting. Therefore, in 60 articles 220 independent fragments were singled out.

Subsequently, an analysis of articles from clinical journals was made. In particular, 77 articles from the journal KHIRURGIYA were subjected to fragmenting. A total of 44 articles lent themselves to fragmenting.[1] Of them 110 independent fragments on 18 aspects were singled out, in particular the "state of the problem," "etiology," "pathological anatomy," "clinical picture," "differential diagnosis," "treatment," "remote results of treatment," "postoperative complications," "prevention of diseases" and so forth. Fragments of such aspects as "treatment" (24), "clinical picture" (14), "etiology" (11), "remote results" (10) and "differential diagnosis" (9) proved to be the most frequent.

The use of formal text signs--markers and indicators identifying various sense aspects (fragments) of documents--facilitates the procedure of extraction of independent fragments (fragmenting of texts). For example, such markers as "picture," "symptoms," "clinical aspects" and "complaints"

1. Among the 33 articles that did not lend themselves to fragmenting it was not advisable to single out fragments from 13 articles of the general type "brief reports," and fragments from 20 articles would not have been understandable outside the context.

can serve as identifiers for the aspect "clinical picture;" "causes," "onset," "consequence" and so forth, for the aspect "etiology." The list of such indicators is given in a special dictionary, where both the equivalence of formal signs and the possible paradigmatic relations among them, for example, "operation-intervention-resection," are taken into account.

The experts and specialists chosen for an evaluation of the independence of the fragments acknowledgedthat they met the requirements. Only one fragment from the journal KHIRURGIYA was rejected as not independent.

The data obtained attest to the fundamental possibility of singling out individual fragments of articles published in physiological and medical journals and of developing on this basis the so-called Fragment subsystem within the framework of an integral information system.

Such a subsystem can be used not only by scientific workers, but also clinicians, for whom, obviously, this is especially important when there is a need for an emergency solution of certain problems connected with treating people.

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PRINCIPLES OF FUNCTIONAL ORGANIZATION OF TISSUE SYSTEMS

Pushchino PRINTSIPY FUNKTSIONAL'NOY ORGANIZATSII TKANEVYKH SISTEM in Russian 1976 pp 2-17

[Preprint of article by V. G. Tyazhelova and I. G. Akoyev, USSR Academy of Sciences Scientific Center of Biological Research, Institute of Biological Physics]

[Text] Analysis of the postradiation kinetics of proliferative systems in the body showed that they can be described rather completely if consideration is given to the average time that cells remain within the system's proliferating, maturing, and functional pools. The ratio taken by these times is a characteristic of the tissue. It is demonstrated that the integral body contains tissues for which the time constants differ by one order of magnitude. Research on systems containing a large quantity of units reveals that in the norm, different body systems are weakly associated with one another. Within a complex system, control functions are applied to one of the units, and they manifest themselves in the unit with minimum time constants. Control may be exercised over different systems exhibiting the same change in the feedback coefficient.

The research presented here would be of interest to radiobiologists and mathematicians dealing with biological problems. The material of this preprint will be discussed in the book "Regulyatsiya protsessov vosstanovleniya" [Regulation of Restoration Processes] (Moscow, Izdatel'stvo Nauka)

The mammalian body is a complex multisystem set (1,2,5). Numerous attempts have been made to date to describe the behavior of the body as a whole and its individual systems using the methods of cybernetics. This research direction has received a special name--"biocybernetics" (3), which is now

developing intensively in entirely different aspects. In the present paper cybernetic methods are used to analyze the unique features of the structure of body tissues, mainly proliferative cell systems. Analysis of the restoration of tissue systems following disturbance of their equilibrium by radiation made it possible to reveal the fundamental principles of tissue system organization and control.

When subjected to destructive effects of internal and external origin, the mammalian body as a whole and its individual systems are able to maintain their homeostasis through a large number of compensatory and regulatory reactions that proceed at different levels of biological organization (4,5). The laws governing organization and work of regulatory systems is the province of the theory of automatic regulation (TAR). If we are to apply it correctly, we must isolate--within the phenomenon under examination--the system subject to regulation, the regulator, and the principle of regulation. This task--defining the units named above--is the object of the first phase of the research--analysis of the biological phenomena. This is followed by mathematical description of the units, the solution process itself, the prediction of system behavior implied by this solution, and the general conclusions.

1. Universal Three-Unit Model of Tissue Functional Organization

The nature of restoration processes is defined in many ways by the inertial characteristics of the pools making them up. Inertial characteristics can be defined as the average time cells remain within the system's dividing, maturing, and functional pools (6-8).

Before we can categorize the diversity of cell forms typical of, as an example, different primordia in bone marrow, into these three pools, we would need to distinguish all of the rather basic phenomena associated with development of blood elements, reducing their number to a minimum in this case. This approach of subdividing cells into pools does not differ from the commonly accepted one of the literature (9).

The objective of our research was to study the functional organization of tissue systems, as it is related to functional stability following disruption of a steady-state condition by radiation, and the precision with which a new steady state is achieved.

This paper generalizes, from these positions, the results of modeling proliferating body tissues, such as the crypt-villus cell system and the hemopoiesis-peripheral blood system, performed earlier with real radiobiological material (6-8).

The cell populations of proliferating tissues are restored through repopulation, which begins at the moment mitotic activity recovers. The end of the mitotic inhibition phase and presence of a sufficient quantity of cells in the different pool systems are the initial conditions of

repopulation. These initial conditions predefine the concrete source of restoration, particularly the minimums of cell numbers in the functional pool--for example in peripheral blood, which is so important to radiation sickness. However, these initial conditions do not predetermine the type of behavior exhibited by the cell system under examination.

Our models were based on the hypothesis that a controlling signal that regulates restoration of a cell system arises in response to this system's failure to perform its function. If we assume that all cells of a functional pool have the same capability for performing their function, we may presume that the body reacts to a below-normal number of cells in the functional pool.

In nonproliferating cell systems, the capability for intensifying a function or compensating for its deficiency is achieved through hypertrophy of the intracellular apparatus. The three-unit model of tissue functional organization developed below is also valid in relation to this approach. It should apply to the turnover of functional protein (secretions) or to the quantity of energy produced (volume and number of mitochondria). A discrepancy signal is received and transmitted by the body's control systems (nervous and endocrine), and it is through this act that negative feedback occurs in the system.

In the first part of the paper we will not dwell on the details of system control. We will assume that the feedback coefficient, k, reflects the presence and effectiveness of certain hormones in the tissue, and that it may vary somewhat depending on various conditions. The rate of cell production is presumed to be proportional to the product of the discrepancy and the size of the feedback coefficient.

Thus the functional pool is the regulated variable, and the proliferating pool is the regulator. The principle of regulation may be stated as control based on the deviation from the required number of cells in the functional pool. We should note that in clinical practice, a normal cell number is defined as the limit toward which the system tends, but one which it does not achieve. Owing to this we have a discrepancy between the actual number of cells and the norm, which is what we need if we are to control the constant activity of the proliferating pool. In order that this state of equilibrium would be maintained, cells must be constantly produced by the system's active element, this process defining the level of mitotic activity of tissues in their normal state.

Basing ourselves on the discussion above, we can rather fully describe the kinetics of the restoration of proliferating tissues by means of a three-unit model involving the following system of equations:

$$\left.\begin{aligned} \frac{dn_1}{dt} &= k(N_3 - n_3)/T_0 - n_1/T_1 \\ \frac{dn_2}{dt} &= \frac{n_1}{T_1} - \frac{n_2}{T_2}; \quad \frac{dn_3}{dt} = \frac{n_2}{T_2} - \frac{n_3}{T_3} \end{aligned}\right\} \qquad (1)$$

Here n_1, n_2, n_3 are the number of cells in the proliferating, maturing, and functional pools, T_1, T_2, T_3 are time constants corresponding to equal times of presence of the cells in the indicated pools, T_0 is the time of cell generation in the proliferating pool, k is the feedback coefficient, t is current time, and N_3 is the required number of cells in the functional pool. Figure 1 is a block diagram of the relationships between the variables.

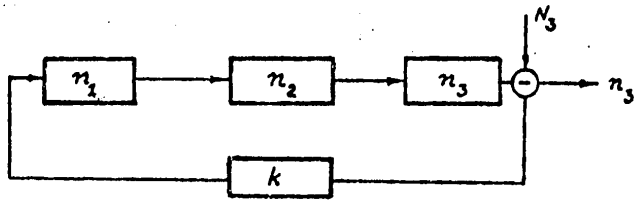

Figure 1. Block Diagram of the Mutual Relationship of Variables in a Three-Unit Model

This is a linear variant of the model, it yields to analytical examination, and it permits us to conceptualize the biological content of its individual components, and evaluate the interaction occurring between different pools of the tissue system.

It should be noted that each pool has its own self-regulation loops, for example the cell contact inhibition system in the proliferating pool, and so on, examination of which would best proceed with isolated cell populations. They will not be examined in this communication, inasmuch as this paper emphasizes control by the body. In the model examined here, cells undergo real movement in the feed-forward circuit as they transform out of proliferating cells into maturing cells and then into functional cells, while real cell movement does not occur in the feedback circuit. It is assumed that the feedback circuit is put into play remotely (from afar) by neurohumoral effectors.

Equation (1) is typical of tracking based on an error--a deviation from a given value (14). The transfer functions for n_1, n_2, n_3 are presented below.

$$\left.\begin{aligned} n_1 &= \frac{N_3 T_1 (1+pT_2)(1+pT_1)}{T_3 (1+T_0/kT_3)\cdot f(p)} \\ n_2 &= \frac{N_3 T_2 (1+pT_3)}{T_3 (1+T_0/kT_3)\cdot f(p)} \\ n_3 &= \frac{N_3}{(1+T_0/kT_3)\cdot f(p)} \end{aligned}\right\} \qquad (2)$$

$$f(p) = 1 + p\frac{T_1+T_2+T_3}{T_0+kT_3}T_0 + p^2\frac{T_1T_2+T_1T_3+T_2T_3}{T_0+kT_3}T_0 + p^3\frac{T_0T_1T_2T_3}{T_0+kT_3}. \qquad (3)$$

Introduction of the transfer functions is a formal procedure in which the derivative symbol in equation system (1) is substituted by the symbol p (that is, the functions are subjected to a Laplace transformation). Thus the system of differential equations is substituted by a system of algebraic equations, and the available TAR apparatus permits us to analyze a number of properties of such a system.

When $t \to \infty$--that is, when $p \to 0$, we can obtain stable values for the variables under examination. Their respective values are:

$$n_1 = \frac{N_3 T_1}{T_3 + T_0 T_3/kT_3}; \quad n_2 = \frac{N_3 T_2}{T_3 + T_0 T_3/kT_3}; \quad n_3 = \frac{N_3}{1 + T_0/kT_3}. \qquad (4)$$

It follows from these expressions that the feedback coefficient, k, defines the stable values of the variables in the system after the transient process ends. A transient process is one in which a system returns to a stable (steady) state following deviation from it. This deviation of the stable value from the one required is what is referred to in the TAR literature as the dynamic error, or dynamic precision.

Usually solution of technical problems requires attainment of rather high precision--that is, minimum error or discrepancy. Formulas (4) illustrate that the precision rises as T_0/T_1 approaches zero--that is, when the feedback coefficient is sufficiently large. As an example were we to limit the precision to 10 percent, then we would need to satisfy the condition $k = 9 \cdot T_0/T_3$. It might be concluded at first glance from the formulas for n_1 and n_2 that the model is imperfect, inasmuch as even in

the limiting case the variables under examination here do not tend toward their required value. Let us return to the initial equations. In a steady state, the rate of transition from one pool into another must be equal, and in view of this the following conditions must be satisfied:

$$\frac{N_1}{T_1} = \frac{N_2}{T_2} = \frac{N_3}{T_3}. \qquad (5)$$

Using (5), we transform the formulas for n_1 and n_2 into the form

$$n_1 = \frac{N_1}{1 + T_0/kT_3}; \qquad n_2 = \frac{N_2}{1 + T_0/kT_3}. \qquad (6)$$

We can see from (6) that the values for n_1 and n_2 are determined with the same precision as that of n_3, and they depend on the length of life of the functional elements, cell proliferation time, and the size of the feedback coefficient. Relationships (5), despite their apparent simplicity, are extremely important. Possessing data on the time cells remain in different pools, we could use relationships (5) to estimate the average number of cells in the different pools and, on the other hand, were we to possess data on the latter, we could determine the time cells remain in the different pools. These relationships are valid, for example, in relation to the red blood system, for which they equal 10^6 cells/24 days = = 10^6 cells/24 days = $5 \cdot 10^6$ cells/120 days (3). Similar relationships are satisfied for the crypt-villus cell system as well: 500 cells/ /10 hr = 500 cells/10 hr = 200 cells/40 hr. The scatter of the values of these parameters is significantly greater for myeloid cells in the white blood system. It can be assumed that the time of presence in the proliferating, maturing, and functional pools is 8, 6.5, and 9.25 days for human white blood, and that the number of cells in these pools is, respectively, $2 \cdot 10^6$, $1.6 \cdot 10^6$, and $7 \cdot 10^3$ (10-13), for which relationship (5) would be satisfied. Such data are absent in the literature for other tissues in view of the complexities of estimating the relationships between the functional, maturing, and proliferating pools, and therefore we did not make the corresponding estimates. It was assumed that the number of cells per unit volume of bone marrow reflects the total number of marrow cells, and that the number of marrow cells reflects the functional potential of the bone marrow. These assumptions are valid after a long postradiation period, and they may be made in steady-state research.

If we agree to the validity of relationship (5), which can be written in general form as $a/b = c/d = e/f$, then $a:c:e = b:d:f$ is valid as well.

It follows from the latter that the ratio of the numbers of cells in the proliferating, maturing, and functional pools, or the ratio of their average times of presence in these pools, may be assumed to be a characteristic of the tissue. Returning to the actively proliferating tissues for which we were able to make this evaluation, we should note that for red blood this ratio is 0.2:0.2:1, both for the number of cells and the time constants of the proliferating, maturing, and functional pools. This ratio is 0.25:0.25:1 for the crypt-villus cell system, and 30:30:1 for white blood. We suggest that these ratios are a significantly meaningful characteristic of the tissue, one which could be used as the basis for computing, with the assistance of the proposed model, the basic characteristics of restoration following a damaging effect.

It is usually difficult to estimate, in experimental analysis of tissues, the proportional content of cells in the proliferating, maturing, and functional pools. It is much simpler to determine the times of presence of cells in the divisions of tissue types, using formula (5) and the transient times of the individual pools of the tissues under examination. For the tissues enumerated above, we found that the first two figures of both of the parameters examined are close. This permitted us to reduce the entire set of tissue characteristics to a single quantitative parameter, a step which turned out to be useful to subsequent analytical examination and analysis of the graphical dependencies. It is entirely possible that the noted law is not universal (we will assess its universality later, after accumulating enough experimental material); however, the found ratios were discovered to be valid in our analysis of actively proliferating tissues. We designated this parameter Q, and we will use it subsequently. As an example, for red blood $Q = 0.2$, and for white blood $Q = 30$.

Equation (1) may be transformed into a dimensionless form to study the relative quantity of cells in the different pools:

$$\frac{dn_1^*}{dt^*} = k^*(1 - n_3^*) - \frac{n_1^*}{T_1^*}; \quad \frac{dn_2^*}{dt^*} = \frac{n_1^*}{T_1'} - \frac{n_2^*}{T_2^*}; \quad \frac{dn_2^*}{dt} = \frac{n_2^*}{T_1} - n_3^*. \qquad (7)$$

Variables marked with an asterisk are transformed values related to the quantity of cells typical for normal conditions:

$$n_1^* = \frac{n_1}{N_1^0}; \quad n_2^* = \frac{n_2}{N_2^0}; \quad n_3^* = \frac{n_3}{N_3},$$

and change in time occurs in relative units of the duration of the functional pool , $t^* = t/T_3$. This transformation also changes the values of the time constants and the feedback coefficient. Capitalizing on the

fact that the tissues are characterized by approximately equal values of T_1 and T_2, and N_1 and N_2, and that the ratio of these parameters to T_3 and N_3 is our parameter Q, we can represent equation system (7) in the following form:

$$\frac{dn_1}{dt} = \frac{k(1-n_3)-n_1}{Q}; \quad \frac{dn_2}{dt} = \frac{n_1-n_2}{Q}; \quad \frac{dn_3}{dt} = n_2 - n_3. \tag{8}$$

The asterisk symbol is dropped from this system. Our subsequent investigation pertains to the dimensionless variant. In this case we adopt the average time of presence of cells in the functional pool as the unit of time. As follows from (8), there is only one variable parameter in such a dimensionless variant for the examined tissue (given a fixed Q)--the feedback coefficient k. This makes it possible, on comparing the restoration process observed experimentally and that obtained by modeling, to determine the strength of the feedback and the degree of its variability in the presence of different pathological situations, using the developed model description of the kinetics.

A digital computer was used to derive the restoration process experienced by different tissues, which will subsequently be referred to as the transient process. We studied recovery of cell composition following a 50 percent reduction of the quantity of cells in the proliferating pool. It follows from expressions (2-3) that in this case the quantity of cells in the functional pool is defined by a third-order differential equation. Depending on the concrete values of the parameters involved, its solution may be the product of three aperiodic units (three first-order systems), or the product of an aperiodic unit and an oscillating unit. Change in the coordinates with time can be described by superimposing the solutions for each of the units. In the first case

$$x(t) = A_1(1-e^{-\frac{t}{\tau_1}}) + A_2(1-e^{-\frac{t}{\tau_2}}) + A_3(1-e^{-\frac{t}{\tau_3}}),$$

and in the second case

$$x(t) = B_1(1-e^{-\frac{t}{\tau_4}}) + B_2\left(1-\frac{e^{-\xi t/\tau_5}}{\sqrt{1-\xi^2}}\cos\omega t\right).$$

Parameters τ_1, τ_2, τ_3, τ_4, τ_5, ω are determined from the roots of the equations corresponding to the transfer function (3). When the time constants of the different components differ by a factor of 5 or 10, the process with the lower time constant may be ignored, since it attenuates much faster than do the other components (14).

Thus to analyze the system we must find the roots of the equation defined by the transfer function, after which it would be easy to reveal the type of transient process involved--that is, the relationship between the oscillatory and aperiodic solutions. To obtain the rootsof the complete cubic equation, we can use an iteration procedure which would allow us to find the roots quickly, with a small number of iterations (14). The following system may be recommended for determining the roots of the equation $a_1p^3 + a_2p^2 + a_3p + 1 = 0$, which may be placed in the form $(1+p\tau)(1 + b_2p + b_1p^2) = 0$; $\tau = a_1/(a_2-\beta)$; $\beta=\tau(a_3-\tau)$. After determining τ, we can compute the parameters of the oscillating unit using the formulas $b_1=a_1/\tau$, $b_2=a_3-\tau$. Considering that the oscillating unit may be more obvious when presented in the form $1 + 2\xi pT + p^2T^2$, where $T = 2\pi/\omega$, we get formulas of the following form for parameters T and ξ:

$$T = \sqrt{\frac{a_1}{\tau}}, \quad \xi = (a_3-\tau)/2\sqrt{\frac{a_1}{\tau}}.$$

Figure 2 shows the results of computing ξ for different values of parameter k. For the sake of visuality, the figure also shows the system precision achieved with the given values of the parameters. As was noted above, the size of ξ reflects the tendency to oscillate. The general solution for the oscillatory unit can be represented in the form

$$x(t) = Ae^{-\frac{\xi t}{T}}\cos\omega t.$$

When $\xi<0$, the exponent transforms from an attenuating one into a growing one, and the process becomes unstable. When $\xi=0$, we are dealing with a purely oscillating and unattenuating process. When $\xi=1$ the oscillatory process transforms into two aperiodic processes exhibiting an asymptotic tendency toward normal. When $\xi=0.3$ a certain number of oscillations occur in the transient process.

An analysis of the curves describing change in the number of cells following irradiation in the blood system and in the crypt-villus cell system would show that as a rule the real transient processes of these systems are oscillatory, and that their ξ is approximately equal to 0.3. The larger the value of ξ, the greater is the system's stability reserve. As follows from Figure 2, the system's precision worsens as ξ rises. Thus the requirements on the system's stability and precision are contradictory, and it would be of interest to reveal which evolution has preferred in real body systems.

As we can see from Figure 2, different systems differ in their capabilities, mainly: A minimum precision may be achieved with a system of 1:1:1 type.

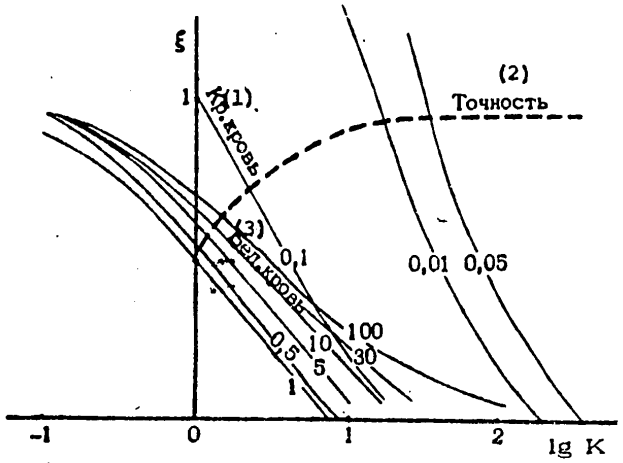

Figure 2. Dependence of Oscillation Tendency and Dynamic Precision in a Three-Unit System on the Feedback Coefficient for Different Tissues

Key:
1. Red blood
2. Precision
3. White blood

The stability boundary is reached in such a system at $k=7$, and the precision attained is 87 percent, while for other work modes in which acceptable stability is insured (a ξ value close to 0.3), the normal value is attained with a precision of about 73 percent. This system is in a sense a boundary system. With all other ratios of numbers of cells and time of presence in proliferating, maturing, and functional pools, the joint characteristics of the transient process worsen. Figure 3 shows the results of determining the roots with oscillatory period and feedback as the coordinates. This figure gives a clearer impression of the way different tissues group together. The upper part of the figure is occupied by tissues for which the period of the oscillatory unit is significantly greater than that of the aperiodic one. The time of presence of cells in the functional pool is low for these systems in comparison with time of presence in proliferating and maturing pools. These systems are stable within in a rather broad interval of values of the feedback coefficient, when the latter is low. The lower part is occupied by tissues for which the oscillatory process transforms into an aperiodic one. Such systems are stable, and their precision is a result a high amplification factor. The middle part of the figure contains a zone within which acceptable transient processes--sufficient precision and low degree of oscillation--are not attained. Also typical of them are comparable values for the time of the oscillatory and the aperiodic unit. It was already noted above that the characteristic number for red

blood is 0.2, it is a value close to that, 0.25, for the crypt-villus cell system, and it is 30 for the white blood system. These real tissues are specially marked in figures 2 and 3. We can see (Figure 2) that despite significantly different numerical characteristics, the white and red blood systems are extremely similar in relation to the parameters of the transient process. Given an identical tendency to oscillate (ξ=0.3), the transient process of these tissues is characterized by the same precision (5 percent) and by different values for the periodicity of the processes (Figure 3).

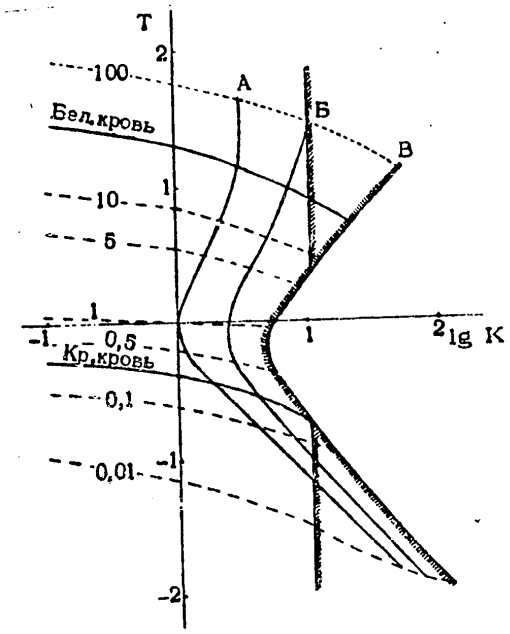

Figure 3. Range of Existence of Quality Indicators of Acceptable Stability and Dynamic Precision (Shaded) in a Three-Unit System

Key:
1. White blood
2. Red blood

If the biological characteristics of the task require that we describe cell differentiation in greater detail, from a mathematical aspect this would mean adding inertial units.

When we go from a three-dimensional to a four-dimensional problem, the controllable variable is now defined by a fourth-order transfer function.

The transient process of such a system is more complex, and it may be represented either as a superimposition of four aperiodic units, or two aperiodic and one oscillatory unit, or the product of two oscillatory units. As in the case of the three-dimensional problem, the form of the process predetermines the relationship between the time constants of the individual units and the size of the overall feedback coefficients for the system. The behavior of the system is described by the following equation system:

$$\left.\begin{aligned} \frac{dn_0}{dt} &= k(N_3 - n_3) - \frac{n_0}{T_0}; \quad \frac{dn_1}{dt} = \frac{n_0}{T_0} - \frac{n_1}{T_1}; \\ \frac{dn_2}{dt} &= \frac{n_1}{T_1} - \frac{n_2}{T_2}; \quad \frac{dn_3}{dt} = \frac{n_2}{T_2} - \frac{n_3}{T_3} \end{aligned}\right\} \tag{9}$$

To investigate the processes, we first analyzed the roots of the fourth-degree equation describing the transfer function corresponding to equation system (9). It was assumed that there were two pairs of complexly conjugated roots. Thus using the iteration procedure we determined T_i and ξ_i, i=1,2. When $\xi > 1$, one of the oscillating units breaks down into two aperiodic ones, corresponding to presence of two real roots. For an equation having the form

$$x_4 + a_1 x^3 + a_2 x^2 + a_3 x + a_4 = 0, \tag{10}$$

the iteration procedure of this approach satisfies the following formulas:

$$\alpha = \frac{a_3}{a_2 - \beta} - \frac{a_4(a_1 - \alpha)}{(a_2 - \beta)^2}; \quad \beta = \alpha(a_1 - \alpha) + \frac{a_4}{a_2 - \beta}.$$

After we determine parameters α and β we write equation (10) in the form

$$[x^2 + (a_1 - \alpha)x + a_2 - \beta][x^2 + \alpha x + \frac{a_4}{a_2 - \beta}] = 0,$$

which leads to

$$T_1 = \frac{1}{\sqrt{a_2 - \beta}}; \quad \xi_1 = \frac{a_1 - \alpha}{2\sqrt{a_2 - \beta}}; \quad T_2 = \sqrt{\frac{a_2 - \beta}{a_4}}; \quad \xi_2 = \frac{\alpha}{2}\sqrt{\frac{a_4}{a_2 - \beta}}.$$

The results of determining parameters T_1, T_2, ξ_1, and ξ_2 are shown in Figure 4. We can see from the figures that the tissues differ significantly in the values of parameter ξ for two second-order units formed in this case (given different sets of time constants for the examined units). In this case ξ is close to 1 for one of the units and depends very little on changes in the amplification factor. For the other unit, ξ changes within broad limits when the amplification factor changes--from 1 to negative values. In essence this unit is the controlled unit, and change in its parameters is precisely what predetermines the type process, the system's precision, and its stability. Figure 4 shows the way ξ for the controlled unit of different tissues depends on changes in the feedback coefficient.

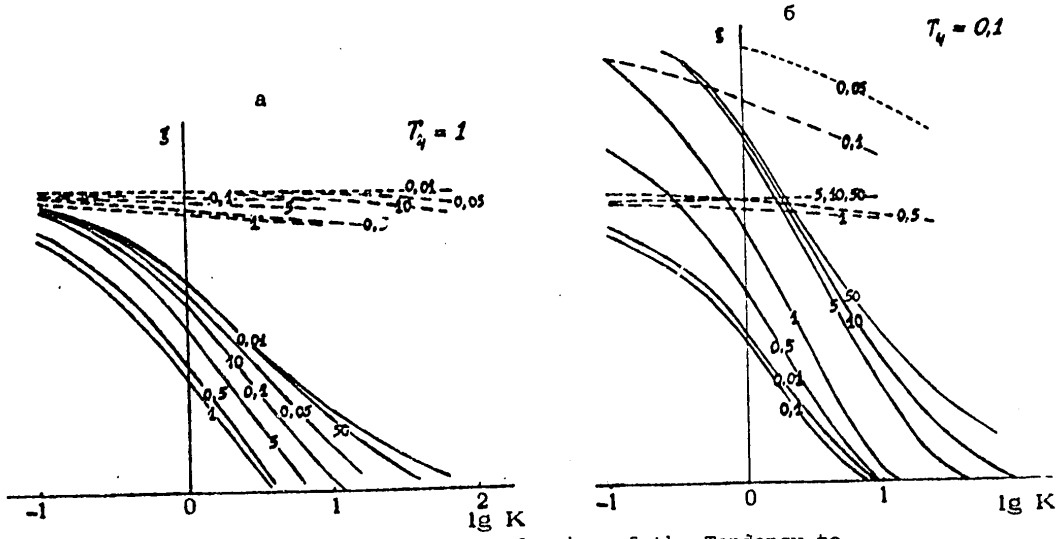

Figure 4. Two Types of Dependencies of the Tendency to Oscillate in a Four-Unit System on the Size of the Feedback Coefficient, for Different Tissues

Computations show that addition of one more inertial unit does not strongly alter the form or type of transient process in the system. It would have a certain influence when entirely different time constants are introduced; if in this case we reduce the matter to splitting one time constant into two, we do not observe fundamental changes in the restoration process. This principle was studied by a modeling technique, as result of which we found that the two transient processes for the number of cells in the functional pool of a three-unit model and a four-unit model, in which the time constant of the differentiating unit equals the sum of the two time constants and $T_2 >> T_1$, are completely identical. It follows from this fact that all processes of cell differentiation in which only quantitative transformation of cells occurs, and not change in the numbers of cells, would best be united into a single unit with a total time constant.

Thus the graph-based computations presented above for the parameters of the asymptotic and oscillatory units, which characterize the quality of the transient process, are universal. A three-unit model can be used to describe the restoration kinetics of different types of tissues. The appropriate figures may be obtained from the graphs presented here, without having to make additional computer computations. For this purpose all we need do is establish the quantitative characteristic of the tissue and use the graphs shown in figures 2 and 3.

The proposed three-unit model permits us to evaluate the role of cell pools in the kinetics of the restoration process, and it helps us to understand the influence each component has upon the type of transient process, on its time, and on the quality indicators, which describe the unique features of system restoration. When involved with the reverse problem, we can use the type of transient process--presence or absence of a tendency to oscillate--and its period as a means to evaluate the ratio of time constants for cells in the three main pools, and to estimate the feedback coefficient. When performing research on real restoration processes occurring over time, for example a year following irradiation, we can make an assessment of the degree of change experienced in the oscillation tendency, which is closely associated with the change in the amplification factor. The latter, in turn, may be associated with the quantity of hormones produced by the body to control restoration of the tissue under examination, and with change in the affinity the tissue has for the hormones.

Our research shows that the functional organization of real tissues is such that different types of tissues may be similar in relation to the parameters of their transient process, despite extremely different initial kinetic relationships (different Q). It was established that actively renewable tissues that actually exist function in such a way that large reserves in system precision and stability do not exist at the same time. The quality parameters systems with close time constants are able to provide for are unsatisfactory, and they apparently

do not exist in real life. Our investigation of the three-unit and four-unit models leads us to the conclusion that only one of the units is apparently responsible for control in complex biological systems.

The proposed model permits us to go on to an analysis of principles of organization of body tissue and system control.

2. Some Questions Concerning Tissue System Control

One unique feature of control in biological objects is the circumstance that the controlling system, as is true for the controlled system, is a physiological and inertial system, and that it is also subject to the action of different injurious agents. When we say controlling system, we imply the nervous and endocrine systems, of which the former is the specific receptor of functional insufficiency of controlled systems and is practically noninertial. The endocrine system basically performs effector functions, being the material carrier of the controlling signals, and therefore it has inertial properties. Endocrine system means in this case the peripheral endocrine glands that participate in regulation of the restoration of cell numbers in different systems (hypophysis, thyroid, adrenal cortex, [one word illegible] glands. The capability the controlling system has for adequately reacting to a signal of functional insufficiency (a discrepancy signal) depends on many factors: the state of the peripheral and central portions of the nervous system, the functional state of endocrine glands, and the possibility for transport of hormones to target tissues.

In contrast to the situation in the first part of this paper, in which the feedback coefficient--the control coefficient--was treated as a constant parameter, k, here it will be treated as a variable, and the dynamics of its variation are described by a three-unit model. Many experiements have been performed to confirm change in the controlling signal in response to different functional states, in response to disturbances of steady state, and in the period of restoration (15, 16). On analyzing the published data we can conclude that the kinetics of the postradiation state of proliferating cell systems and the quantity of hormones functioning in [one word illegible] following irradiation are similar in many respects Three pools of cells can be distinguished in actively proliferating cell systems. We can distinguish three basic stages in the controlling system: synthesis of the secretions, their maturation in colloid form, and their transport through the blood system. It is on the basis of this division that we applied the previously proposed three-unit model to describe the kinetics of the quantity of hormones operating during restoration as the controlling factor. This approach significantly broadens the possibility for studying and predicting the behavior of the systems under analysis. This model of controlling and controlled systems contains [one word illegible] units, its block diagram is shown in Figure 5 and its function can be described by equation system (11):

$$\frac{dn_1}{dt} = k_1 \cdot m_3 (N_3 - n_3) - \frac{n_1}{T_1};$$
$$\frac{dn_2}{dt} = \frac{n_1}{T_1} - \frac{n_2}{T_2}; \quad \frac{dn_3}{dt} = \frac{n_2}{T_2} - \frac{n_3}{T_3}; \qquad (11)$$
$$\frac{dm_1}{dt} = k_2 (M_3 - m_3) - \frac{m_1}{T_4};$$
$$\frac{dm_2}{dt} = \frac{m_1}{T_4} - \frac{m_2}{T_5}; \quad \frac{dm_3}{dt} = \frac{m_2}{T_5} - \frac{m_3}{T_6}.$$

Here, n_1, n_2, n_3--number of cells in the proliferating system under analysis present in the proliferating, differentiating, and functional pools respectively; T_1, T_2, T_3--equivalent to the average time of presence of cells in these pools of the system; m_3--specifically the controlling factor, which reflects the quantity of hormones present in blood; m_1--quantity of secretions produced by endocrine organs; m_2--quantity of secretions maturing in colloid form; M_3--prescribed concentration of hormones in the body; T_4, T_5, T_6--average times of presence of secretions in a state of synthesis, maturation, and in functional state; k_2--control system's feedback coefficient, characterizing the degree of control over secretion, which may be oriented toward a normal or a higher level depending on the body's needs; k_1--coefficient characterizing the degree of affinity of peripheral tissues to hormones, which experimental data indicate does change (17). Equation system (11) defines the following form of transfer functions:

$$n_3(p) = \frac{A}{f_1(p)}; \quad n_2(p) = A \frac{T_2}{T_3} \frac{1 + pT_3}{f_1(p)};$$
$$n_1(p) = A \frac{T_1}{T_2} \frac{(1 + pT_2)(1 + pT_3)}{f_1(p)}; \quad A = \frac{N_3}{1 + \frac{T_6}{k_1 M_3 T_3} + \frac{1}{k_2 M_3 T_3}};$$
$$m_3(p) = \frac{B}{f_2(p)}; \quad m_2(p) = B \frac{T_5 (1 + pT_3)}{T_6 \cdot f_2(p)}; \qquad (12)$$
$$m_1(p) = B \frac{T_4}{T_6} \frac{(1 + pT_5)(1 + pT_6)}{f_2(p)}; \quad B = \frac{M_3}{1 + \frac{1}{k_2 T_6}};$$

$$f_1(p) = [(1+pT_1)(1+pT_2)(1+pT_3)(1+pT_4)(1+pT_5)(1+pT_6) + k_2T_6(1+pT_1)(1+pT_2)(1+pT_3) + M_3k_2T_6]/(k_2T_6 + M_3k_2T_3);$$

$$f_2(p) = 1 + p\frac{T_4+T_5+T_6}{1+k_2T_6} + p^2\frac{T_4T_5+T_4T_6+T_5T_6}{1+k_2T_6} + p^3\frac{T_4T_5T_6}{1+k_2T_6}.$$

Using formulas (12) with $p \to 0$, it would be easy to determine parameters m_3 and n_3 following the end of a transient process--that is, the new value of the variables under examination which would be typical of the new steady state:

$$n_3(\infty) = \frac{N_3}{\frac{T_6}{k_1M_3T_3} + \frac{1}{k_2M_3T_3}}; \quad m_3(\infty) = \frac{M_3}{1+\frac{1}{k_2T_6}}. \qquad (13)$$

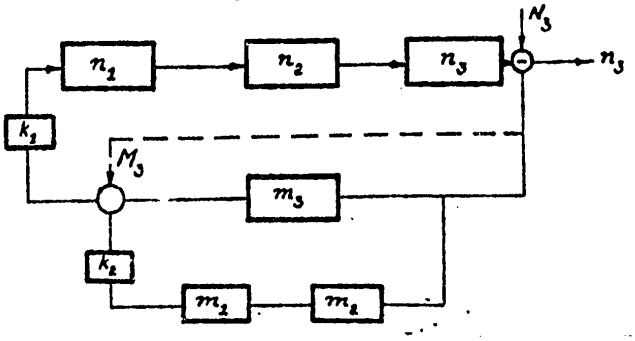

Figure 5. Block Diagram of the Mutual Relationship Between Variables n and m

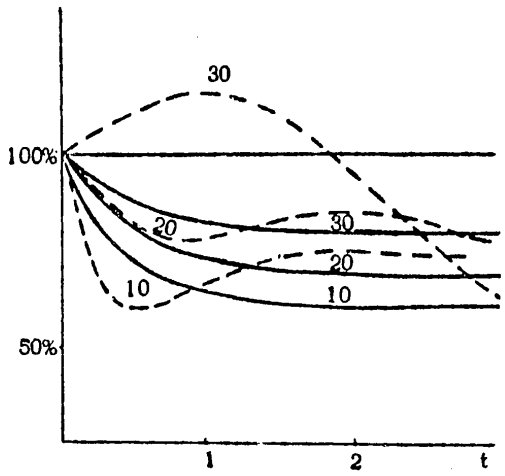

Figure 6. Transient Processes for Variables m_3 (Solid Curves) and n_3 (Broken Curves) at Different Feedback Coefficient Values

A rather good approximation to the prescribed value may be made for variable m_3, which reflects the quantity of the controlling factor corresponding the body's needs; the accuracy of this approximation is governed by the product k_2T_6. The analysis of the transient process for m_3 is described completely by the three-unit model. The nature of the dependencies is significantly more complex for the controlled variable, n_3. Even when the prescribed value of M_3, the amplification factor for the loop of variables $n_i (i=1,2,3)$, is rather high, the limiting value for n_3 would not be satisfactory, if we exclude from the examination parameter k_1, which in biological terms reflects the affinity of acceptors in the tissue under examination to the hormone--that is, sensitivity to the hormone. When $k_1 >> (M_3T_3)/T_6$ sufficiently good accuracy is insured for the system, which can be seen from a comparison of the two formulas in relationship (13). On the other hand change in parameters k_1 and k_2 reflects the body's controlling hormonal influence upon the tissue.

Figure 6 shows, as an example, transient processes for n_3 and m_3 depending on different types of control, in the presence of variations in coefficient k_1 and k_2. We can see from the figure that the effect of the mentioned factor varies. When k_1 is constant and k_2 grows, the level toward which the aperiodic process associated with n_3 tends rises. When the tissue's sensitivity to hormones rises significantly, the transient process for n_3 transforms from an aperiodic to an oscillatory process; as k_1 grows, the tendency to oscillate rises, the system's precision improves, and periodicity of the processes decreases. It should be noted that the conclusions implied by an examination of the transient process for a six-unit system coincide completely with conclusions made from the analysis of the three-unit system.

The active elements in this model are the system of proliferating cells in the system under analysis, and synthesis of secretions in the controlling system. A value proportional to the sum of the squares of the rates of proliferation or synthesis may serve as an estimate of energy expenditures in both loops of the model under examination.

The investigation showed that the sum of the rates for variables m_3, written as Σv_2^2, varies approximately in proportion to the square of the change in parameter k_2, and that it does not depend on k_1. The sum of the squares of the proliferation rates, Σv_1^2, is proportional to the square of change in k_1, and it exhibits approximately a linear dependence on change in k_2. It follows from this analysis that the greatest energy expenditures are associated with growth in tissue sensitivity to hormones (coefficient k_1), and that growth in the coefficient describing feedback in the controlling system (coefficient k_2) has a lesser influence.

It was already noted that joint satisfaction of system precision and stability requirements raises contradictions as a rule. A high feedback coefficient insures greater precision for the system, but it may lead to an unstable situation (small or large values of ξ). Compromise may be achieved in satisfying the system stability and precision requirements through exercise of a certain quality of the system. As was shown above for third-order systems, close feedback coefficient values impart an acceptable quality to different body tissue systems (ξ=0.3 and $\Delta\leqslant$15 percent). By varying its value we can change the quality of the system; system stability is the more critical parameter in this case.

A six-order system may also be used to represent mutual behavior of two three-unit controlled systems. In this case the type of relationships existing between systems changes in comparison with the variant examined above, as does the material expression of the feedback coefficient, but the type of transient process and the quality of the more-complex system would be described, as before, by a six-order equation. Let us analyze the roots of the sixth-power equation in the same way that we did with the third- and fourth-power equations. We will seek, for the sixth-power equation,

$$x^6 + a_1 x^5 + a_2 x^4 + a_3 x^3 + a_4 x^2 + a_5 x + a_6 = 0$$

three pairs of complexly conjugated roots using the following iteration procedure:

$$\alpha = \frac{a_5}{a_4 - \delta} - \frac{a_6(a_3 - \gamma)}{(a_4 - \delta)^2}; \quad \beta = \alpha(a_1 - \alpha) + \frac{a_6}{a_4 - \delta};$$

$$\gamma = \alpha(a_2 - \beta) + \frac{a_6(a_1 - \alpha)}{a_4 - \delta}; \quad \delta = \alpha(a_3 - \gamma) + \frac{a_6(a_2 - \beta)}{a_4 - \delta}.$$

After determining these four parameters we can write the initial equation in the form

$$(x^2 - \alpha x + \frac{a_0}{a_4 - \delta})\left[x^4 + (a_1 - \alpha)x^3 + (a_2 - \beta)x^2 + (a_3 - \gamma)x + a_4 - \delta\right] = 0,$$

and apply to it the iteration procedure used earlier with the fourth-order equations.

The results take the form of three pairs of values for T and ξ, which are shown in Figure 7 and in the table. It follows from the figure and table that the six-unit model contains two second-order units, the parameters of which depend little upon change in the amplification factor, and that only one of the units is oscillatory, and actually controllable. An analysis of the results showed that the system's behavior depends on more than just the ratio of the time constants. Thus for example when all of the time constants are increased by one order of magnitude, no change occurs in ξ and, consequently, in the quality of the system, while the values of all of the determined T increase by an order of magnitude.

Parameters Resulting From Solution of the Six-Unit Model

Tissue	T_1	ξ_1	T_2	ξ_2	T_3	ξ_3
1,1,1,1,1,1	1,62	0,98	1,2 ÷ 1,5	0,82÷0,65	0,53÷0,58	Variable
1,1,1,1,1,.1	1,33	0,98	0,90	0,91	0,25÷0,4	
1,1,1,1,.1,.1	1,14	0,99	0,88	0,98	0,104÷0,221	
1,1,1,..1,.1,.1	1,1	0,99	0,38÷0,53	1,4 ÷1,02	0,08÷0,145	
1,1,..1,..1,..1,.1	1	1	1,48÷2,36	0,95÷0,86	0,07÷0,095	
1,..1,..1,..1,..1,.1	0,4	1,43	0,138	0,87	0,059	
1,100,100,100,100,100	145	0,97	98÷118	0,919÷0,73	1,08÷3,33	
1,1,100,100,100,100	107	0,99	9,34	0,99	1,05÷1,89	
1,1,1,100,100,100	101	1	11,9÷16,8	4,12÷2,96	0,86÷1,61	
1,1,1,1,100,100	100	1	1,45÷2,26	0,96÷0,89	0,72÷1	
1,1,1,1,1,100	12,7÷14,5	4	1,33÷1,7	0,89÷0,78	0,61÷0,65	

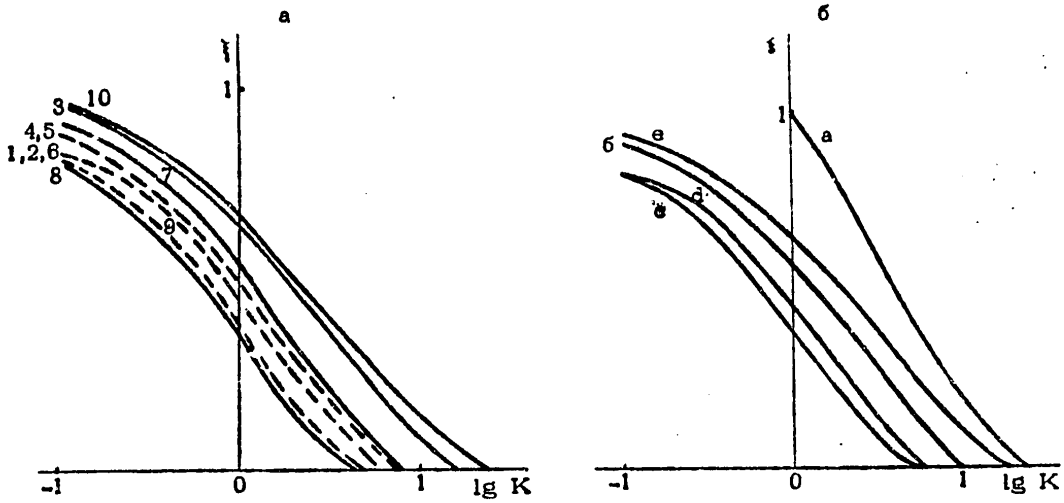

Figure 7a. Dependence of oscillation tendency in the controlled unit of a six-unit system on the feedback coefficient for tissues characterized by different sets of time constants. *1*--six time constants have the same value; *2*--five time constants have the same value and one is an order of magnitude larger than the rest; *3*--four time constants are the same and two are an order of magnitude larger; *4*--two triplets of time constants differing by one order of magnitude; *5*--four time constants are the same and two are an order of magnitude lower; *6*--five time constants are the same and one is an order of magnitude less; *7*--five time constants are the same and one is two orders of magnitude larger than the rest; *8*--four time constants are the same and two are two orders of magnitude larger; *9*--two triplets of time constants differing by two orders of magnitude; *10*--four time constants are the same and one is two orders of magnitude lower than the rest; *11*--five time constants are the same and one is two orders of magnitude lower than the rest.

Figure 7b. Change in oscillation tendency upon transition from a three-dimensional model (*a*--tissue with time constant set 0, 1, 0.1, 1) to a four-dimensional model (*b*--tissue with time constant set 0.1, 0.1, 1, 0.02-0.5) and a six-dimensional model (*c*--tissue with time constant set 0.1, 0.1, 1, 0.2, 0.4, 0.6; *d*--tissue with time constant set 0.1, 0.1, 1, 1, 50, 50; *e*--tissue with time constant set 0.1, 0.1, 1, 10, 10, 10; *f* [sic]--tissue with time constant set 0.1, 0.1, 0.1, 0.1, 0.1, 0.1)

We can conclude from the data presented above that when we analyze complex interacting body systems, we need not examine cumbersome multidimensional models, and the practical control boils down to changing the minimum number of parameters. Inspection of the parameter values depending on change in the amplification coefficient would show that those tissues for which the inertial characteristics of the systems are the same or close provide the worst conditions for the transient process. Maximum mutual influence of units is typical of such systems; when we examine intersystem interactions, we find that maximum mutual influence of systems is typical. A more-detailed analysis of the three-unit system led to the conclusion that such systems cannot insure normal conditions for tissue existence, and this is probably why they do not exist in nature. Applying this result to intersystem interactions, we could say that strongly interacting systems are apparently excluded from the body.

Comparative analysis of the found roots of the third-, fourth-, and sixth-power systems shows that as we rise up the ladder of system complexity, we find that those with highly different time constants are the best. As the system becomes more complex this requirement becomes more and more significant. As the number of units rises, a stable process establishes itself at lower values of the amplification factor which may be uniquely associated with deterioration of system quality due to a decline in dynamic precision (see Figure 7b, curves *a*, *b*, *c*, *d*, *e*). The smaller the difference between time constants, the lower is the quality of the system, and the greater they are, the higher the quality. Systems with all time constants the same are of the same quality, irrespective of the values of these parameters. If differences exist in the time constants, that system in which one parameter is larger than the others would be the worst, and the system in which one parameter is distinguished by being lower than the rest is the best (see Figure 7a).

As we proceed from third-order systems to fourth-order systems and then to sixth-order systems, the controlled system ceases to be aperiodic, and it basicaly becomes oscillatory (parameter ξ in the controlled system remains less than unity with all values of the feedback coefficient). If the time parameters of the individual units differ, the quality of the system depends mainly on the time constants with the small values (see table). This is also valid in relation to intersystem interactions.

The two premises formulated above--that control is exercised by a single unit and that the strongly interacting units are excluded--are associated with one another. The more the systems differ, the greater is the probability of separating out the one that is in fact the controlled system in the body, and of controlling it, and that control will be exercised through the unit in this system having the least inertia.

Figures 7a and 7b illustrate that different body systems group together rather closely in relation to controllability. We may say that there exists a range of controllability in which change in the feedback coefficient does not cause deterioration of system quality below an acceptable value.

As the system becomes more complex the controllability range grows narrower and shifts left, which now leads to quality deterioration. To keep the quality the same in such a case, we would have to have an even greater difference (more than an order of magnitude) in the system's time constant (Figure 7a). The fact that the controllability range narrows as the number of units in the system rises permits the hypothesis that there is a limit to both its breadth and the amount it shifts. This limit should not differ strongly from that associated with the controllability range of really existing body tissues, which are approximated rather satisfactorily by third-order systems. The fact that the controllability range does grow narrow, that it tends toward a limit, and that the real body contains only those systems which simultaneously exhibit acceptable precision and stability, and the fact that different body systems possess similar quality characteristics all leads to the conclusion that given identical change in the feedback coefficient, systems that are entirely different in relation to their time constants and their complexity may be controlled identically.

The analysis presented here leads to two generalizations pertaining to the principles of functional organization of real tissues.

1. The principle of economy of organization: That units of a complex controlled system have parameters in the presence of which the functional of the dynamic error, the system's stability reserves, and the energy cost of maintaining the system in a sufficiently stable state are minimized in relation to the feedback coefficient.

2. The principle of economy of control: No matter how complex the biological system under examination is, its parameters assume their values in such a way that control is exercised through the first- or second-order unit exhibiting the least inertia, and the parameters of the different body tissues are such that when identical changes occur in the coefficient of control, the quality of the different systems changes in about the same way.

Conclusion

Our work permitted us to formulate the following premises.

When complex multiunit systems consisting of controlled and controlling or of interacting controlled systems are modeled, only those for which the time constants differ significantly are stable. In fact, the time the cells remain in different cell pools differs significantly in real body tissue systems.

As the complexity of the system grows (as the number of units or number of systems increases), the degree of difference in the time constants must grow, and this in the end implies a need for relative independence of the systems. This means that in a normal situation, interaction

between different tissue systems in the body must be minimum. If such interactions do arise by necessity (for example following partial depopulation of a tissue system), the time cells remain within the newly switched-in systems (or the rates of certain processes) must differ considerably from what is true of the system under analysis.

The stability of a system is defined by the units with minimum time constants, given identical feedback coefficient values. It follows from this that in the case of controlling restoration of cell numbers, the controlling influence manifests itself mainly in the units in which cells spend the least time.

When intersystem interactions are involved the controlling influence manifests itself to a greater degree within the system for which the overall time constant is minimum. Such a system is more sensitive to change in the controlling signal.

The first phase of research on the principles of functional organization of body tissue systems has been completed. By approximating their behavior with just a linear three-unit model, we can reveal a number of fundamental aspects of both the structure and the control of tissues; this, we believe, paves the possible ways for directed influence upon body tissue systems. We feel that research on the limiting possibilities of a system and establishment of the laws governing hierarchical subordination of tissues will permit us to deepen our developing ideas, and gain a clearer idea of the laws governing the relationships among the body's numerous systems.

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EFFECTS OF RADIATION ON DNA

Moscow RADIATSIYA I DNK (RADIATION AND DNA) in Russian 1979 signed to press 28 Feb 79 pp 2, 3-4, 190-191

[Annotation, Introduction and Table of Contents from book by N. I. Ryabchenko Moscow, Atomizdat, 1,750 copies 191 pages]

[Text] Annotation. The book analyzes the action of ionizing radiation on the structure of the DNA macromolecule. It examines current methods of analysis of injuries to the primary and secondary structures of DNA and, also, of injuries of desoxyribonucleoprotein complexes. It treats analysis of mechanisms of radiation damage to the macromolecular organization of DNA during its irradiation in model experiments and as a part of the makeup of biological specimens. Results are presented of studies on repair of various types of injuries to the DNA structure (single-strand and double-strand breaks, damaged bases, DNA-membrane complexes) in irradiated bacteria and mammalian cells.

The book is designed for radiobiologists, biphysicists, biochemists and specialists interested in problems of injury and repair of the structure of DNA.

Introduction. A very important task of current radiobiology is the study of trigger mechanisms of the lethal and mutagenic action of ionizing radiation. A series of radiobiological studies have shown that injury to the unique controlling systems of cells plays a decisive role in the development of radiobiological reactions, leading to death of the cells, to occurrence of gene and chromosome mutations. According to current concepts, the function of controlling systems is realized by DNA macromolecules. In the light of what has been presented above, there is great interest in studies which deal with the action of ionizing radiation on the structure of the DNA macromolecules both in model experiments and as part of the makeup of biological specimens.

It is possible to represent the overall scheme of organization of DNA in the cell as follows: DNA + protein→desoxyribonucleoprotein→macromolecular structures, in the form of which DNA exists in the cell. Radiation can act upon the individual molecules of DNA and protein, upon the bond of protein with DNA in the DNP, and, also, lead to disruption of the supermolecular structures (complexes of DNA-protein-membrane).

A very important injury of the primary structure of DNA is disruption of the integrity of its polynucleotide chain as the result of appearance of single-strand and pair breaks. According to modern concepts, pair breaks are lethal for the cells while single-strand breaks, remaining unrepaired, can lead to the occurrence of additional pair breaks. Ionizing radiation not only disturbs the integrity of the polynucleotide strands but, also, affects the nitrogen bases. The result of the irradiation can be chemical modification of the structure of the bases and, also, rupture of the N-glycoside bond with subsequent removal of a base from the DNA polymer. Arising stable modifications of the bases, and a-purine or a-pyrimidine particles, can serve as a substrate for specific endonucleases, the ultimate result of whose action is enzymatic single-strand breaks. Under the action of ionizing radiation, disturbance also occurs of the ordered secondary structure of DNA which is the consequence of the radiation-chemical damage to the primary structure of the DNA.

Reports of many investigators have shown that the fate of the primary damages of genetic structures, their realization in important damages of chromosomes, or inactivation of cells, depends on the course of subsequent biochemical processes which are able not only to increase the number of primary injuries in the DNA but, also, to lead to their repair. Data available in the literature on post-radiation modification of injuries to the DNA structure testify, also, to the substantial contribution of enzymatic processes to the determination of the final outcome of the radiation damages to the DNA.

In connection with the fact that the integrity of DNA is vital for cells, we felt it was expedient to examine the current status of the problem on types of injuries which arise in radiation of DNA, methods of analysis of these injuries, and, also, paths of enzymatic repair and additional pre-affection of DNA in cells of bacteria and mammals. This book also deals with analysis of these problems.

The author expresses sincere thanks to A. M. Poverennyy, A. S. Sayenko, B. P. Ivannik, V. G. Skvortsov and P. I. Tseytlin for help in carrying out the experimental studies and discussion of individual sections of the book.

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INTERACTION OF ULTRASOUND WITH THE BIOLOGICAL ENVIRONMENT

Pushchino VZAIMODEYSTVIYE UL'TRAZVUKA S BIOLOGICHESKOY SREDOY (Investigation of the Mechanisms of Biological Effects of Ultrasound) in Russian 19/9

/Annotation and table of contents of book/

/Text/ This collection contains original studies of Soviet and non Soviet scientists, devoted to the study of the biological effects of ultrasound action and mechanisms, providing the basis for the effects produced and also to the study of acoustic properties of biological objects of different levels of organization: from solutions of low molecular derivatives of proteins and nucleic acids up to tissues.

The book is intended for a wide range of specialists: biophysicists, biologists, physicians, acoustics' scientists and physiochemists.

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INTERACTION OF DIFFERENT SYSTEMS UNDER RADIATION INJURY (Theoretical Prerequisites and Models)

Pushchino MEZHSISTEMNYYE VZAIMODEYSTVIYA PRI RADIATSIONNOM PORAZHENIYI (Interaction of Different Systems Under Radiation Injury) in Russian, 1978

/Annotation and introduction from book. Editors, Doctor of Biological Sciences I.G. Akoyev and Candidate of Technical Sciences, V.G. Tyazhelova. Editor of this issue - Candidate of Technical Sciences V.G. Tyazhelova/

/Text/ This collection presents investigations of problems of mutual connection of systems in the proximate and remote periods after radiation effects. Special attention is given to the mutual connections of controling and controlled systems. The collection presents, for the first time, material concerning the sequence of inclusion of reserves during prolonged and intensive processes of recovery which makes possible correct, subsequent theoretical and mathematical modelling. A mathematical model of cell proliferation is proposed. Peculiarities of injury and recovery of individual systems of the organism under different influences are analyzed. Some mechanisms and results of the influence on biological objects of high-frequency, electromagnetic and magnetic fields are examined.

The collection is intended for radiobiologists, biophysicists, pathophysiologists and mathematicians, involved in the study of theoretical biology.

Introduction

Among the different problems of theoretical biology, a special place is occupied by problems of pathology of man and mammals, caused by extreme states according to the massiveness and practical significance of these states. Among the factors which create extreme situations, the most frequent are physical factors: different forms of corpuscular and electromaguetic radiations (from ionizing radiation up to radio frequencies), magnetic, acoustic effects, etc.. Key aspects of this problem are

associated with the most general processes of formation of pathology in the individual organism. The relative internal temperature, the biochemical and genetic constancy, inherent to each individual, lightens this task.

Radiation injury of the organism caused by high energy ionizing radiation is a good model for study of the general pathological principles. It is well known that primary radiation injuries arise in all structures and tissues of the organism. Further development of the injuries and the transition of them into observable pathological changes depend upon the structural-functional peculiarities of physiological systems, on their inherent capacities for development of compensatory--restorative reactions at all components of their levels of biological integration.

This makes it possible to proceed, on the basis of a study of changes which arise and the effect of ionizing radiations, to a theoretical investigation of the most general principles of development of pathology and the interaction of biological systems of different complexity in the organism in the normal state and under extreme situations, caused by different factors. An example of such an approach is the concept developed by us concerning vicious pathogenetic circles which explained how, on the basis of seemingly insignificant changes of functional activity of some systems, serious disturbances of the interconnection of many systems of the organism and the transition of prepathogenetic states into the clinical manifestation observed may result.

Problems of correct theoretical modelling of processes with mathematical analysis of mutual connections and phenomena have great significance for theoretical generalizations. This thematic collection is a second edition of the USSR Academy of Sciences of the Scientific Center of Biological Researches and also considers theoretical prerequisites and problems of mathematical modelling of radiation injury of the organism and its systems. In distinction to the first edition, issued in 1975, in which great attention was given to the posing of problems and the development of theoretical prerequisites to modelling, this edition contains extensive consideration of problems of interaction between systems and to the use of mathematical modelling for detection of disturbances or the arisal of new connections between systems. These problems are investigated as nonspecific in relation to the concrete form of the factor which affects the organism.

At the same time, the explanation of primary mechanisms of effect of different factors, especially the explanation of the effect of electromagnetic fields, is of great interest.

The generality and difference of mechanisms of influence on the organism of different physical factors represent some of the vital questions of today's science. Therefore, this collection contains some studies which reveal peculiarities of the effect of electromagnetic fields on model, primary biological structures. The results cited in this may provide some of the departure points for revealing the mechanisms of injury to the organism under the effect of electromagnetic radiation on it.
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LABORATORY DIAGNOSTICS FOR TOXIC POISONING FROM PESTICIDES

Moscow LABORATORNAYA DIAGNOSTIKA INTOKSIKATSIY PESTITSIDAMI in Russian by 1978 signed to press 6 Mar 78 pp 2, 3-6, 128

[Annotation, Introduction and Table of Contents from book by Ye. N. Burkatskaya, G. G. Lysina, and V. N. Karpenko, 4000 copies, 125 pages]

[Text] The book, summarizing data from the literature and experimental studies, presents the principles and methods of laboratory diagnostics for toxic poisoning from pesticides. An attempt is made to correlate data on the biochemical, hematologic and clinical-physiologic shifts in experimental animals and humans exposed to pesticides used in agriculture.

Based on laboratory studies, a brief summary of the toxic properties, the mechanism of toxicity and the clinical picture of toxic poisoning from pesticides is given. An analysis of the diagnostic significance of different functional indices for toxic poisoning by pesticides is given. In addition, the most sensitive and informative tests for early diagnosis of poisoning from pesticides of various chemical structures and toxicity are discussed. The use of laboratory studies during periodic medical examinations of individuals working with pesticides in order to monitor the state of health during intensive seasonal work on farms is recommended. An index of methods is outlined to distinguish pesticides in various biospheres. Literary references are also provided. Physiologic norms are described for aid in identifying undesirable effects of pesticides on an organism.

The book is written for professional pathologists, doctors in clinical laboratories, sanitary-epidemiological stations and clinicians in various specialties, concerned with the problem of pesticides.

Introduction

The last decade has been characterized by intensive development of the chemical industry and the wide spread utilization of chemical substances in all areas of industry and agricultural production. The use of chemical substances to protect plants (pesticides, toxic chemicals) in agriculture has grown by 140%. The general consumption of chemical and biological substances per hectare of cultivated field has increased during a 10 year period from 81.2 to 135.1 kg.

The increase in use of pesticides can be illustrated by the following figures: if in 1966-70 after the effects of pests, disease and weeds, production of various agricultural crops was worth on an average of 4.9 million rubles yearly then during the last five years more than 6 million rubles worth of crops were cultivated and in the Tenth Five Year period one can expect to obtain an additional yearly production value in a sum of 8.5-9 million rubles.

Introduction into man's environment of chemical substances with various degrees of biological activity can lead to disturbance in the ecology of the environment, the occurrence of acute and chronic poisoning, debilitating forms of toxic poisoning, changes in immunobiologic reactivity of an organism, an increased level of general illness, a decrease in work capacity, development of long-range complications and other harmful effects. The undesirable effects of pesticides can be detected in individuals working directly with them, in people living in proximity to individuals who process pesticides, in laborers who work in fields adjacent to areas of pesticide application, in those individuals responsible for maintenance of the treated field and in those involved in processing of the harvest which contains residual amounts of pesticide. The possibility exists for penetration of pesticides in food products of a vegetable or animal origin.

With the wide spread use of pesticides and the resolutions of the Twenty Fifth Congress of the Communist Party of the Soviet Union to develop prophylaxis for occupationally induced disease, the question of opportune and correct diagnostics for toxic poisoning has acquired special urgency.

Effective prophylactic measures include preventative and periodic medical examinations.

Hygienic norms for storage, transportation and application of pesticides (toxic chemicals) in agriculture (No. 1123-73 put into effect on September 20, 1973) have been formulated for work with pesticides to insure the health of individuals. Periodic medical examinations are important both for prolonged contact with pesticides and for individuals involved in seasonal labor.

Limits for length of time that laborers are allowed to work with pesticides are defined by lists of contraindications outlined in public health laws.

Medical examinations are conducted in a number of regions throughout the country where there is an intensive use of pesticides. Results of these exams showed the inadequate estimation of the influence of occupational factors. Medical examination are conducted often only by therapeutists who do not utilize specialized laboratory analyses. For adequate and correct diagnosis of toxic poisoning by pesticides data obtained by hematologic, biochemical, electrophysiological and other methods of analysis are very important.

Oriented to the practical requirements of the therapeutic-prophylactic establishments in the Ukrainian SSR, we developed in 1970 a compilation of methodologic directions entitled "Laboratory Methods for Conducting Medical Examinations on Individuals Working with Toxic Chemicals." This index received praise from public health organs. These directives helped to improve the quality of medical examinations in the republic. However, this brief summary of methodologic directives did not provide a complete representation of the related materials and numerous data found in the literature on methods of laboratory diagnostics for toxic poisoning from various pesticides. During recent years, new information has been gathered on this question requiring correlation and analysis of material to define the most important diagnostic laboratory tests.

In attempts to correlate data on laboratory diagnostics for toxic poisoning from pesticides, in writing this book the authors used the categories of volume of application of various preparations, the degree of toxicity and danger and prospects for their future utilization. Substances are enumerated which are used widely in agriculture and authorized for experimental production use ("Index of Chemical and Biological Means to Control Pests, Plant Diseases and Weeds," recommended for use in agriculture during 1976-77).

The effects of biopreparations (arenarin, bactorhodeucide, boverin, dendrobacillin, trichothecin, phytobacteriomycin, entobacteria) are not discussed because there is an essential difference between the effect of biopreparations and chemical substances on the human organism and warm blooded animals. The clinical influence of biopreparations includes allergenic symptoms, disturbances in immunologic reactivity and others. The long-range consequences (carcinogenic, teratogenic, embryo-toxic and gonado-toxic effects) and the diagnostic indices for pathology have different significance and deserve separate examinations.

New pesticides recommended for experimental production use (acetellic, anilat, baiyalan, delan, calyxin, mezaronil, prefix, tachigaren, EF-2) and those presently used (butylcaptax, 2M-4XP, camparol, caragard, patorin and others) are not included in the book because the future of their use in USSR agriculture is unclear and data from laboratory studies does not exist.

Information on laboratory diagnostics for toxic poisoning from some pesticides is extremely limited, contradictory or entirely absent. In a number of cases only experimental data exist.

Given the continuous flow of new information on pesticides, it is difficult to understand all the data, especially the recent information published on this topic. The authors' aim is to show the need to use laboratory studies during medical examination of individuals working with pesticides, to correlate in an understandable way the diverse material on laboratory diagnostics for practicing medical personnel, to organize medical examinations and to select indices for evaluation of the state of health of exposed individuals based on laboratory studies.

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IV. PHYSIOLOGY

EVOKED POTENTIALS IN PSYCHOLOGY AND PSYCHOPHYSIOLOGY

Moscow VYZVANNIYE POTENTSIALY V PSIKHOLOGII I PSIKHOFIZIOLOGII in Russian 1979 signed to press 29 Dec 77 pp 2, 3-4, 212-213

[Annotation, foreword and Table of Contents from book by E. M. Rutman, Moscow, "Nauka," 1979 216 pages].

[Text] The book reviews data accumulated during 30 years of application of the method of recording evoked potentials (EP) from the surface of the human brain. Results of studies conducted during the last five to ten years using VP in psychology and psychophysiology are discussed in depth.

The difficulties, limitations and possible future uses of the method are examined. Attention is directed at current methods for analysis of recorded EP and the neurogenesis and functional meaning of separate components are reviewed. Information on the morphology of EP derived from widely differing types of scimuli are presented.

The publication is intended for psychologists and psychophysiologists and will also be of interest for neurophysiologists, psychiatrists and neurologists.

The book contains six tables, 21 illustrations and a bibliography of 642 references.

Foreword

Recording of evoked potentials (EP) from the brain surface in man opened up a new and indispensible "window on the brain." The method, first used in 1947, was applied in many areas in 1960s and continues to be developed rapidly at the present time. It has been utilized to resolve an ever expanding number of problems in the most diverse fields of psychology and psychophysiology and has been applied in studies on the nature of EP, their relation to brain structures and functions. Concurrently, new methods to record and analyze EP have been developed. However, the literature reviewing all the above-mentioned directions is difficult to locate. Investigators who hope to utilize this method or decide on the expediency of its use for specific problems, must be familiar with current concepts on the nature of EP and must have adequate methods for analysis of existing data as well as new results. The purpose of this monograph is to familiarize the investigator with current concepts on this topic.

The book is divided into three sections. In the first section, genral methodologic questions are examined with particular attention directed at the complex and not completely understood problems of the method (neurogenesis, variability, evaluation methods, etc.). A short history of the development of the method and the changes in concepts of the neurogenesis of EP components is presented. The importance of a critical approach to the data in the literature and the need for strictness in interpretation of results is stressed. The need for psychologists and psychophysiologists to be familiar with current neurophysiological studies on the nature of EP and concepts on the relationship of waves recorded from the brain surface to the activity of brain structures is underscored. A large part of this section is concerned with current methods for mathematical elaboration and a multi-dimensional analysis of EP recordings.

The second section of the book contains information on the morphology and neurogenesis of modal specific components of EP in response to auditory, visual and somatosensory stimuli. Normative data are presented on the morphology of EP, induced by basic forms of stimuli used in experimental studies. In addition, changes in EP are examined in relation to modal nonspecific character stimuli (probability stimuli) and the magnitude of interstimuli intervals.

The third section presents a short synopsis of current studies using EP in the fields of psychology and psychophysiology. Fundamental accomplishments, possible causes for failure of the method and prospects for future studies are examined.

Publication of several monographs (Shagass, 1975; Ivanitskii, 1976; Kostandov, 1976; Beteleva et al, 1977) related wholely or partially to the method of VP and its application in a number of fields has helped to resolve some but not all questions related to this method. These publications have contributed possibly to some unevenness in the interpretation of the data, but on the whole seem to be sound and have proved to be correct.

The author would like to express deep gratitude to I. V. Rabich-Shcherbo for his helpful participation in the writing of the book.

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PSYCHOPHYSIOLOGICAL ASPECTS OF ULTRA-SLOW BRAIN RHYTHM ACTIVITY

Moscow PSIKHOFIZIOLOGICHESKIYE ASPEKTY SVERKHMEDLENNOY RITMICHESKOY AKTIVNOSTI GOLOVNOGO MOZGA in Russian by N. A. Aladzhalova in Russian 1979 signed to press 27 Feb 79, pp 2, 3 - 5, 213 - 214

[Annotation, introduction and annotation from monograph by N. A. Aladzhalova, Izdatel'stvo "Nauka", 4,100 copies, 216 pages]

[Text] This monograph is devoted to the study of ultra-slow bioelectrical activity in the human and animal brain, to developing the concept of a slow cerebral regulating system and rhythm as a factor in the spontaneous regulation of psychic functions.

Introduction

This monograph describes the spectrum of infra-low frequencies and bioelectrical activity in the human and animal brain. The frequencies in this spectrum are lower than the frequencies familiar in electroencephalography and have been given virtually no study in comparison with the latter. At the same time, the psychic processes of man are subject to infra-low frequency fluctuations (variations in attentiveness, the thresholds of perception and the like). The need for reliable knowledge of human behavior demands a detailed psychophysiological study of infra-low-frequency phenomena.

This book differs in content from our previously published monograph, "Slow Electrical Processes in the Brain" [4]. Where the basic content of the preceding monograph was an analysis of the physiological mechanisms of the ultra-slow cerebral potentials discovered in experiments on animals, this project shifts the accent to the questions of the relationship between the ultra-slow potentials of the brain and changes in the level of stimulation and various manifestations in the activity of human consciousness. The most troublesome issue in the modern study of the brain — the question of the relationship between physiological and psychic activity — is studied from this point of view.

A certain universal biological rhythm has stood out among the psychic processes as well as in the bioelectrical cerebral phenomena as the general order

of nature. A question has arisen as to the role of cyclic processes in the brain as well as in psychic phenomena, in regulating the functional states and their transformations and in the regulation of mental activity. This statement of the problem takes us away from the theories of traditional electroencephalography since infra-low periodicity is not explainable by the individual properties of a neuron or the sum total of them but occurs as a new characteristic of group combination or a collective form of involvement in common objects of regulation.

The functioning of a neuron depends on interaction with the immediate surroundings, that is, on physical proximity to them and on the range of symbolic or impulse forms of communication. Because of the effective communication in group combinations of neurons, general types of reactions can develop although some have a well-established pattern, that is, the ability for flexible communication is lost. Various patterns of neuron interaction in groups are nothing other than a collective form of their involvement in common tasks of regulation. Adjacent elements of the neuronal ensemble subject to different communications networks can develop different forms of response and selectively accept sources of information. However, the channels of communication are not only the routes of contact but are also the products of communications control. A number of communications channels exist that are unequal in stability, size and effectiveness. Coordinating them is one of the tasks of regulation.

Functional systems are a world of orderly mutual responses whose structure insures the achievement of a goal and arise in the process of regulation while the limitations of the system are determined by the ranges of effective communications. These functional systems vary in structure, size and the territorial distribution of their components. Some are small and concentrated while others are extensive and their parts widespread; some consist of relatively homogeneous populations while others are extremely mixed; they differ in the breadth and definition of their boundaries — the components of some systems can operate in a closed circuit but organizations with a large number of random and variable participants are also possible. Characteristics functions exist within each functional system, specific activations that have been categorized take place and, while acquiring a symbolic form, different orientations develop even though each element of a given system can become involved in another or in even several systems. On one hand, barriers form in each system against free exchange with others and this is a property of the organizational structure; these barriers break down temporarily only in crisis situations. On the other hand, free exchange is always present within the confines of specific levels.

Ultra-slow periodicity stands out as a factor of functional dynamics whose basis is an exceptional capacity for flexible coordination, the development of new forms of cooperation. A regular fluctuational process is one of the mechanisms involved in the coordination of functional elements. Spontaneous rhythm in a broad spectrum characterizes cerebral development and, specifically, the fluctuation in potentials with periods equal to seconds, minutes and hours. Because the biopotential waves properly follow each other within a system, predicting the activity that can be expected from the environment is made easier.

Ultra-slow fluctuations in cerebral potentials reflect the activity of the brain's slow control system which insures hemispheric restructuring of the activity level in conjunction with the functioning of the mechanisms that maintain stability and homeostasis. They also reflect the mechanisms that form the foundation for transformations in functional states and conversions to new levels of activity.

B. F. Lomov [49] believes that any juxtaposition of the totality of mental and elementary neurophysiological processes must be done through analysis of the overall cerebral, integrative and systemic processes. The ultra-slow rhythmic fluctuations in brain potentials combine the activity of elements in some vast dynamic organization while acting as hemispheric coordinators. This level of integration is elevated to a higher specialized cerebral process.

The primary problem of psychophysiology is to determine how the cerebral processes and psychological functions are coordinated among themselves. This book examines this coordination through experimental analysis of the ultra-slow cerebral potentials and psychological data.

Our new research into the genesis of ultra-slow brain potentials in animals is examined in the first five chapters. The forms of interaction among the ultra-slow potentials and neuron impulses and their role in coordinating neuron activity are defined by means of the statistical method of analysis. The spectrum of ultra-slow fluctuations in the human brain and its basic patterns are examined in Chapters 6 - 9. Altered states of consciousness are studied during sleep, under hypnosis and during monotony. Human functioning is investigated in the process of arbitrary mental tasks, in the automation of mental activities and during the process of intuitive activity and in other situations.

The studies of ultra-slow rhythmic fluctuations in brain potentials were made at the Institute of Psychology, to some extent at the USSR Academy of Medical Sciences Institute of Neurology and at the Laboratory for Clinical Neurology directed by Professor F. V. Bassin.

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FORMATION OF A BIOPOTENTIAL FIELD IN THE HUMAN BRAIN

Leningrad FORMIROVANIYE BIOPOTENTSIAL'NOGO POLYA MOZGA CHELOVEKA in Russian 1979 signed to press 2 Jul 79, p 2, 3 - 4, 163

[Annotation, introduction and table of contents from book by A. N. Shepoval'nikov, M. N. Tsitseroshin, V. S. Apasionok, "Nauka", 163 pages]

[Text] In a study of the static and dynamic properties of the brain's biopotential field in children and adults, patterns of quasi-periodic change were observed in the phase gradients of the dominant EEG waves. Some of the functional properties associated with the direction of phase leadership are described. It was established that the probability of maintaining a specified phase structure increases in proportion to growth in a child. Information is presented as to the new generalized statistical characteristics of the brain's biopotential field that points to an increase in the stability of the center-to-center connections with growth in children and the delayed rates of forming these indicators for the state of stimulation in comparison with sleep, especially orthodox sleep. The quantitative indices from an equipment reading on the depth of sleep for a given EEG evaluation during the course of the experiment are examined. A statistical connection is noted between the value of the center-to-center correlations and the length of the latent period for an elementary conditioned motor reflex response to a flash of light. Phenomena are described that are observed in response to testing in the setting of a "controlled experiment" based on the automatic evaluation of the spatial-phase structure of the brain's biopotential field.

Introduction

The problem of the progression of neural processes, knowledge of the mechanisms that insure the functional interaction of distantly discrete brain structures and the integration of their functioning are among the cardinal issues of neurophysiology.

Theories as to the possible mechanisms of neurokinetics and their significance in the organization of cerebral functioning have been advanced by N. Ye. Vvedenskiy (1892), I. P. Pavlov (1913, 1926) and A. A. Ukhtomskiy (1923, 1937a). New findings in neurology and especially evidence as to the important role of

convergence in the brain's biopotentials as a means of evaluating the interaction of the cerebral structures (Livanov, 1962, 1972; Adey Walter, 1963) provide a basis for viewing the temporal and spatial relationships of the brain's bioelectrical activity as an index that will make it possible to make a judgment as to the dynamics of the neural processes.

"Consciousness appears to me to be the neural functioning of a specific portion of the great hemispheres at a given moment and in a given set of conditions which has a known optimum (this will probably be a moderate) degree of excitability.... The portion with optimum functioning is not, of course, a fixed area; conversely, it shifts continuously over the entire expanse of the great hemispheres as a function of the connections that exist between the centers and is under the influence of external stimuli. Appropriately, of course, the range also varies with reduced excitability.

"If we could see through the skull and if the expanse of the great hemispheres with the optimum level of excitability were illuminated, we could see how this imaginary lighted area which is irregular in shape and surrounded by a more or less definable shadow throughout the remaining hemispheric expanse and which is continuously changing in form and value moves about over the great hemispheres in a thinking conscious man." So clearly and figuratively did I. P. Pavlov (1913, pp 174-175) describe his concept of the dynamics of the center-to-center processes.

To what extent can modern neurophysiology confirm or deny this bold suggestion from I. P. Pavlov as to the organization of the interaction between the neural centers? There is not as yet any unequivocal or exhaustive answer since the answer to this troublesome question is to a large extent the solution to the problem of the organizational principles of cerebral functioning. Nevertheless, the facts that have been compiled as to the patterns of distribution for stimulation and inhibition within the nervous network and the reflection of these patterns in the spatial and temporal characteristics of the EEF make it possible to note interesting and important parallels between the systemic reorganization of the brain's biopotential field and certain manifestations of neuropsychic activity.

Progress in the field of studying the local activity of the brain in recent years has clearly slowed somewhat in spite of improvement in the procedures for the automatic processing of the EEG. Obviously the information obtained through analysis of the separate bioelectrical processes do not functionally insure an evaluation of the dynamic interrelationship between remotely discrete structures even when the level of precision is high and this is especially important for the manifestations of the integrative activity of the brain.

The effort to seek out general patterns of spatial and temporal, and especially the phase relationsyips in the fluctuations of the brain's biopotentials is a follow-up to the relatively early efforts in electroencephalography. It is sufficient to note the studies of Motokawa (Motokawa, 1944; Motokawa,

Tuziguti, 1944) made in the mid-1940's where the major patterns of the spatial and phase structures of the waves in the brain's biopotential field were described and the tendency to sustain a relatively stable phase gradient among the dominant EEG waves were noted. An intensification of research into the temporal and spatial relationships among the brain's biopotentials has been conducive to expanding the methodical possibilities brought about by the use of toposcopes and computers during experiments.

Research done under the guidance of Academician M. N. Livanov has had a major significance for the increase in attention to the problems of studying the brain's biopotential field. Founding his position on the classic premises of domestic physiology and primarily on the work of N. Ye. Vvedenskiy and A. A. Ukhtomskiy in regard to the isolability of the nerve centers and the role of "functional resonance" in the neurophysical mechanisms of their "cooperative stimulation", M. N. Livanov has creatively developed the concept of the major role of convergence in the fluctuations of biopotentials for distantly displaced brain structures in reflecting conditions favorable to the generation of intercentric connections.

The fruitful outcome of analyzing the time and space "patterns" of the brain's biopotential processes has been convincingly demonstrated in a study of the formation of neuronal ensembles during the process of realizing the complex forms of activity present in man (Bekhtereva et al., 1977) and animals (Kogan, 1974a, 1974b).

These studies whose importance cannot be exaggerated have provided a means for seeking out the purely electrophysiological correlatives of conditioned-reflex and behavioral reactions and, in fact, have defined one of the main directions of development for modern electroencephalography.

Up until now, many of the properties of the brain's biopotential field in man have been entirely without study or have been inadequately investigated. Among them are the quantitative characteristics of the spatial structure of the amplitudinal and phase distribution of EEG waves, the patterns of constancy and variation in the statistical characteristics of the brain's biopotentials at various levels of stimulation and the importance of changes in the direction of the gradient of phase shifts in EEG waves. The significance of the functional role of comparatively stable phase shifts among the dominant fluctuations in the EEG in man in distantly discrete structures is also unclear.

Where information on these questions is extremely scanty and fragmented, the age characteristics of time and space properties in the EEG are essentially undescribed even though this evolutionary approach to studying the mechanisms for organizing the systemic functioning of the entire brain would prove especially fruitful in this case. A direct association between the spatial characteristics and specific functional processes as well as between behavioral responses and the gradual morphological maturation of the structures responsible for generating the brain's biopotentials during stimulation and sleep would also be important.

There is reason to assume that the disruptions in the integrative activity of the brain that can be associated with damage to the mechanisms for coordinating the intercentric relationships can be found o n l y through a study of the time and space relationships of the EEG whereas recording local electrical activity of even a number of areas will not make it possible to find pathological changes.

All these considerations have prompted us to investigate the basic statistical characteristics of the brain's biopotential field and the temporal-spatial and phase relationships of fluctuations in the EEG waves during various functional states in children and adults.

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CSO: 1840

UDC 57.04 Ch-48

THE FOREBRAIN AND ELEMENTS OF BEHAVIOR

Kiev PEREDNIY MOZG I ELEMENTY POVEDENIYA in Russian, 1978 signed to press 29 Dec 77, pp 2, 3-4, 174

/Annotation, Introduction and Table of Contents from book by V.A. Cherkes, Kiev, "Nauk dumka," 1978, 176 p/

/Text/ This monograph acquaints the reader with the physiology of those higher levels of the brain which are combined into the concept "forebrain." It presents a detailed consideration of existing theoretical ideas concerning complexes of structures or systems directly or indirectly participating in the morpho-functional organization of the forebrain with concentration on contradictions in these ideas. The thesis is advanced that, at the basis of organization of the forebrain of mammals, including man, should be placed a single principle, that is, a unified stable structure and a scheme of such a complex is proposed. In addition to this basic theme, the book also presents some material concerning problems of doubtless interest. It presents data concerning the structural base of some complex forms of behavior, concerning peculiarities of the neuronal organization of the main structures of the forebrain, concerning the development of these structures at different stages of evolution of species and pathologies of structure of the forebrain. The main course of exposition contains some brief historical information concerning the study of the forebrain.

The book is intended for use by physiologists, morphologists, neuropathologists and psychiatrists. 18 illustrations, 1 table, 335 references.

Introduction

The brain functions as a unified entity and its inexhaustible complexity detracts the investigator from this postulate, causing him to study the brain according to its parts. However, the more anatomical structures involved simultaneously in the process of a study, the more completely the activity of the brain is revealed.

The study of the brain according to its parts is unavoidable rather than necessary and this circumstance becomes more appreciable the higher the phylogenetic level of the brain being studied. If the highly specialized and specific centers of the brain stem correspond to a strictly specific function, then in higher supra-stem sections, such a relationship is impaired and it may seem that anatomically separated structures are functionally unified or, on the contrary, anatomically unified structures are functionally separated. In the eyes of an architect, such a construction would be illogical. This is precisely the situation in respect to the complex of those structures which are unified under the concept "forebrain." The laws of development of species, from the pre-vertebrates to the lower vertebrates and from them to the mammals, will assist in the understanding of these features of the morpho-functional organization of the forebrain. This problem is given special attention in this book. In the course of many years of study of a small group of intracerebral nuclei (basal gangliae) we encountered, every time, difficulty when there arose the necessity to determine the main trend of activity of this group as a whole. Possibly, the number of anatomical links in this case was inadequate to reveal their function. Being limited by this, the researcher's opportunities were also limited. We may be assured that, at the higher brain structures, there are other complex structures, the anatomical composition of which does not conform strictly to the physiological make-up.

All of these considerations impelled the undertaking of an analysis of voluminous experimental and, in part, clinical material relating to practically all structures of the forebrain. The course of this analysis and some preliminary conclusions will be presented in the following chapters.

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AUTOWAVE PROCESSES AND CARDIAC ARRHYTHMIA

Moscow VESTNIK AKADEMII NAUK SSSR in Russian No 1, 1980 pp 6-11

[Article by V. I. Krinskiy, doctor of physicomathematical sciences]

[Text] There are widely known examples of processes, in which waves are propagated without damping: burning of Bickford safety fuse, propagation of nerve impulses and waves of excitation in the heart. The main features of such waves are determined by environmental parameters, and they are unrelated to initial conditions. By analogy with autooscillatory processes, which take place in a concentrated system, such processes in a distributed system were called autowaves.

Academicians A. N. Kolmogorov, I. G. Petrovskiy, Ya. B. Zel'dovich and his school, as well as I. S. Piskunov and D. A. Frank-Kamenetskiy, have studied comprehensively wave processes as they relate to propagation of flames and diffusion problems, where they are discribed by equations of the parabolic type:

$$\frac{\partial E}{\partial t} = D\frac{\partial^2 E}{\partial x^2} + f(E). \qquad (1)$$

All these problems have been solved for waves of transfer from one state to another in a one-dimensional environment, where the class of autowave processes is relatively poor: there are only traveling waves here.

We shall discuss in the following a new class of autowave processes recently discovered in similar systems, systems with recovery. A fire in the steppe is an example of such a process: some time after the fire grass will grow again. To equation (1) another equation is added, which describes recovery, and the system acquires the following appearance;

$$\begin{cases} \frac{\partial E}{\partial t} = D\left(\frac{\partial^2 E}{\partial x^2} + \frac{\partial^2 E}{\partial y^2}\right) + f(E, g) \\ \frac{\partial g}{\partial t} = \varphi(E, g). \end{cases} \quad (2)$$

For systems with recovery [or restoration] in the case of two dimensions, a new class of solutions was found, which predicts the existence of turning spiral waves (SW) and guiding [leading] centers (GC (Figure 1).

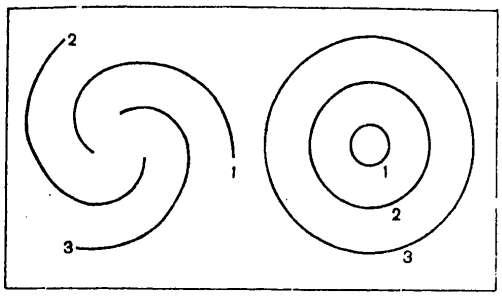

Figure 1.
Turning [rotating] spiral wave (a) and guiding center (b). The numbers refer to the successive positions of the wave

Such autowaves may occur in an environment where there are no auto-oscillatory elements (special point is stable). Each element can merely generate an impulse and then return to a state of rest. The phase plane of a concentrated system is of the Van der Paul type (in Figure 2c, the trajectory on the phase plane is illustrated).

An impulse can be evoked again only after the recovery processes are terminated. In biology, this recovery [restoration] process is called "refractoriness" [?--refractiveness]. In the case of the fire in the steppe, refractoriness (time when the grass grows out) constitutes 1 year, and for the myocardium it is fractions of a second (200 ms). On the phase plane, refractoriness corresponds to segment BCO of the phase trajectory (see Figure 2c), excitation corresponds to AB and the state of rest to point 0 and its immediate vicinity.

There are basic differences between waves in excitable environments[1] and ordinary additive waves (sonic, electromagnetic). When two waves are propagated toward one another, they do not traverse one another like sound waves, but are damped when they meet. This occurs becasue there is propagation of a refractory tail behind the front of excitation, where the points are not excitable (see Figure 2b). For the same reason, the waves are not reflected from the boundaries of the medium. If

one were to excite (for example, start a fire) some elements of the environment, a wave will travel over the environment and then a state of rest will be restored. But SW or GC appear under certain special initial conditions, and from them there will be periodic propagation of excitatory waves.

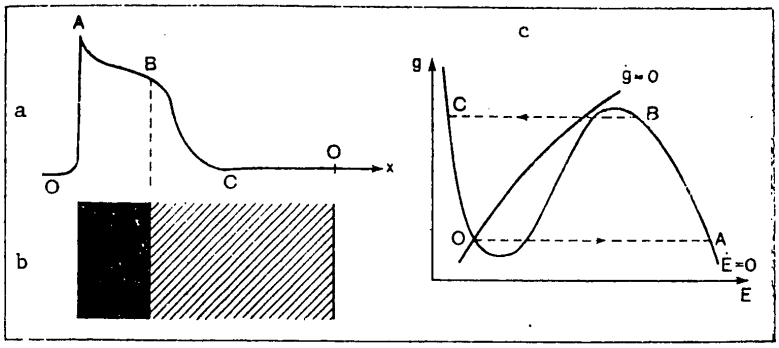

Figure 2. Wave of excitation

a) profile of membrane potential as wave propagates in cardiac tissue
b) diagram of a wave (excited segments are blacked in and refractory ones are cross-hatched)
c) trajectory representing points on the phase plane of the concentrated system corresponding to equations (2); AB segment of the trajectory corresponds to state of excitation, BCO to refractoriness and O with its immediate surroundings to a state of rest.

It is logical to assume that such autowaves exist in systems of any physical nature, for which the phase plane of their equations is of the Van der Paul type. Indeed, both types of autowaves (SW and GC) were experimentally demonstrated in an excitable chemical medium about 5 years after they were theoretically predicted.[2]

For a model of cardiac tissue, the variables in equations (2) and in Figure 2 have the following physical meaning: E--membrane potential (mV), g--conduction of slow component of ion current (Ohm^{-1}). For an excited chemical medium, E is the concentration of Br^{-} ions and g is the concentration of $Fe^{(3+)}$. In spite of the difference in physical meaning of the variables, the phase planes of both systems (cardiac membrane, excited chemical medium) turned out to be similar, and it is not surprising that the same type of autowaves were demonstrated in them.

Occurrence of such autowaves is one of the important mechanisms of impairment of stability in active distributed media [environments].[3] Let us illustrate this on the example of excitatory waves in the myocardium.

The heart contracts about once per second; each contraction is induced by a wave of electric excitation that travels through the heart from the pacemaker (sinus node). After the excitatory wave there is restoration of a state of rest. This mode of wave propagation is so stable in the sense of resistance to perturbances that it provides for reliable heart function for many years.

However, the stability can be impaired. One of the most dangerous disturbances is ventricular fibrillation, with which there is disappearance of synchronized contractions of individual cells and the heart stops pumping blood. Fibrillation is one of the causes of lethality of, for example, myocardial infarction.

The main features of cardiac fibrillation can be attributed to the appearance of many spiral waves in the myocardium. Spiral waves can appear under certain special conditions. In particular, there must be a break in the wave front for them to appear. But in homogeneous media, the waves propagate without breaks; breaks can occur when waves spread in a heterogeneous media.

Figure 3 illustrates two waves propagating in a medium that is heterogeneous for refractoriness; the wavelength varies in different places. As a result, the second wave delivered rather close to the first one could be broken (see Figure 3b). Spiral waves can develop from this break (Figure 4).

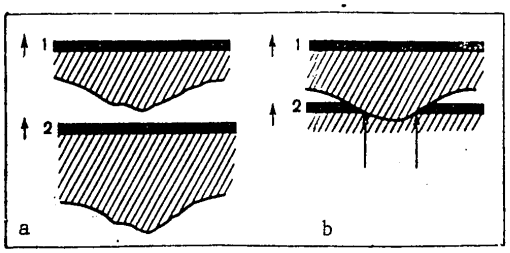

Figure 3.
Occurence of break in a wave

a) normal propagation of waves with large intervals between them (no breaks occur)
b) second wave following the first at an abnormally short distance; breaks occur in the second wave (shown by arrows) in areas where recovery processes had not been terminated after passage of the first wave; excited areas are in black and refractory ones are cross-hatched

Let us describe the mechanism of reproduction of spiral autowaves.[4] Since the period of the turning spiral wave equals the refractoriness, the waves propagating from it follow one another closely, breaking on heterogenous sections (see Figure 3b), and they form the spiral wave as shown in

Figure 4. As a result, the spiral wave appearing in the heterogeneous environment may generate new spiral waves (Figure 5). Let us mention that spiral waves should not multiply in a homogeneous environment (as was observed in the excited chemical medium).

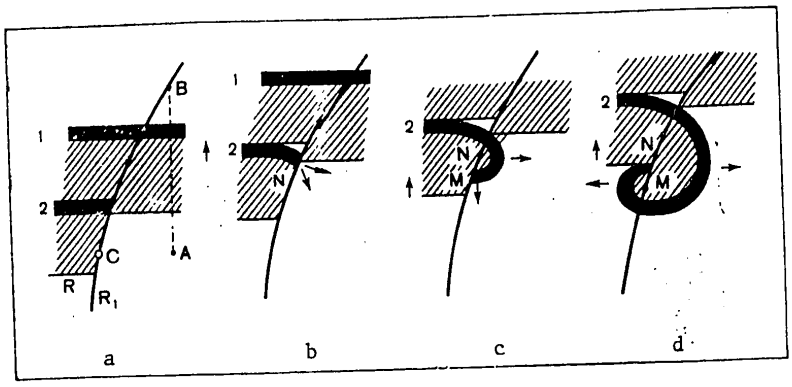

Figure 4. Appearance of spiral wave upon diffraction by wave break of a segment with increased refractoriness.

Refractoriness is less marked on the left (R) than on the right (R_1); excited regions are blacked in and refractory ones, striped; the arrows show the direction of wave movement.

a) wave 2 moves only in the left region; on the right the front of wave 2 excitation runs into the longer refractory tail of wave 1
b) wave 2 moving along the boundary between two regions (BC) lags behind wave 1 (wave 1 travels to point B over the shortest route AB, while wave 2 travels over the longest CB); the front of excitation of wave 2 begins to come in contact with resting segments of the right region at point N
c) excitation from wave 2 spreads to the right region; at point M it can again pass into the left region
d) the wave has passed into the left region, and a spiral wave was formed

Mathematical analysis of the spiral waves revealed that their life span is finite in heterogeneous media. For this reason, there is competition between two processes in the environment: reproduction and extinction [dying] of autowaves. The final type of mode expressed in the environment depends on the proportion between the rates of these processes. If the rate of reproduction V_r is greater than the rate of extinction V_e, the number of sources in the environment may begin to grow and a chaotic process of wave propagation would develop in it. In the opposite case

($V_r<V_e$), a state of rest is restored in the medium, and modes similar to fibrillation are impossible. Here, the critical values of characteristics arise, after exceeding which complex modes become possible. One example of such characteristics is the "critical fibrillation mass," or maximum mass of cardiac tissue with which fibrillation is still impossible.

Analysis was made at the Institute of Biological Physics of the life and time of appearance of spiral waves, rate of reproduction and extinction of spiral waves, time and critical mass of fibrillation.

These results were used, in collagoration with the Scientific Research Institute for Biological Testing of Chemical Compounds, USSR Ministry of the Medical Industry, to develop a method of screening drugs that prevent cardiac arrhythmia. Heretofore, antiarrhythmia products had been developed on a purely empirical basis, according to end effect.

On the basis of the analysis, a simple, dimensionless criterion was proposed, which is the ratio between two typical variables and permits evaluation of the possibility of spiral waves in cardiac tissue. The appearance of spiral waves in cardiac tissue is impossible with $\beta<\frac{1}{2}$ and they can arise with $\beta>\frac{1}{2}$. Experimental investigation of the main antiarrhythmia compounds used in our country revealed that they reduce autowave criterion β. The fact that compounds referable to different classes reduce the same autowave criterion apparently signifies that, in spite of different points of attack, the end result of their action is the same: blocking of spiral waves.

In another series of investigations, studies were made of the effects of several products that provoke arrhythmia, and it was found that, in conformity with the autowave theory, these products raised the value of autowave criterion β.

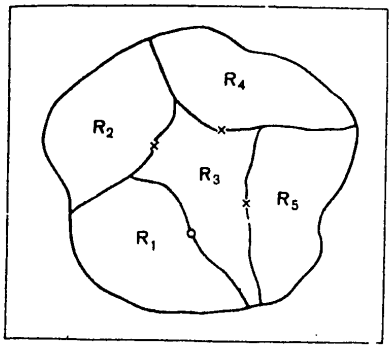

Figure 5.
Heterogeneous environment, in which reproduction of spiral waves is possible

R_1, R_2, ...) refractoriness in different regions

0) site of one spiral wave; the waves it generates will break at the boundaries between regions with different parameters and cause appearance of new spiral waves (see Fig. 3 and 4)

×) possible sites of generation of these waves

The submitted results serve as additional important confirmation of the autowave theory of arrhythmia. In addition, they can serve as the basis for rational screening and development of new antiarrhythmia compounds. We hope that the described types of atuowave processes will be important, not only in biology and medicine, but other branches of science and engineering related to distributed active media.

* * *

After delivery of V. I. Krinskiy's paper, it was submitted to discussion.

G. R. Ivanitskiy, corresponding member of the USSR AS [Academy of Sciences], observed that studies of atuowave processes in distributed biological systems began at the Institute of Biological Physics, USSR AS. in the 1960's. G. R. Ivanitskiy stressed that by now two major results have been obtained in this area. The first explains the cause of cardiac fibrillation and makes it possible to predict the antiarrhythmia products that will prevent it. The second demonstrated the possibility of autowave processes in chemical media. At the present time, this work is well-known abroad, and it is generally recognized that the Soviet Union was the first to achieve this. G. R. Ivanitskiy proposed that research on autowave processes conducted by biophysicists, physicists and chemists be coordinated, since in spite of the differences in phenomena studied their mathematical description turns out to be the same, and advances in one area could aid in development of another.

Yu. V. Gulyayev, corresponding member of the USSR AS, stated that autowave media can be created in solid-state electronics, making use of various properties of semiconductors. Such media have a frequency spectrum ranging from a few hertz to hundreds of megahertz, which makes it possible to develop generators operating in this range. The parameters of such autowave systems can be readily controlled by means of electrical, magnetic fields and other factors. Work dealing with development of various electronic devices based on autowave media are being developed intensively in recent times at the Institute of Radio Engineering and Electronics, USSR AS.

L. A. Piruzyan, corresponding member of the USSR AS, stressed that the processes discussed are interesting from the standpoint of general laws that can be applied in both physics and biology. This research aids in development of a new field, molecular pharmacology. The possibility of controlling autowave processes in the body by means of exogenous factors is also very important.

Academician A. P. Aleksandrov, president of the USSR AS, summarized the discussion and congratulated the authors for obtaining interesting results, wishing them continued major success in development of this important direction.

FOOTNOTES

1. N. Wiener and A. Rosenblueth, ARCH. INST. CARDIOL., Mexico, Vol 16, 1946, pp 205-265.

2. I. S. Balakhovskiy, BIOFIZIKA [Biophysics], Vol 10, 1965, pp 1063-1067; V. I. Krinskiy, in "Problemy kibernetiki" [Problems of Cybernetics], Moscow, Vyp 20, 1968, pp 59-80.

3. B. I. Krinskiy, in "Problemy kibernetiki," Moscow, Vyp 20, 1968; A. M. Zhabotinskiy, "Concentrated Oscillations," Moscow, 1974; R. Z. Sagdeyev, in "Voprosy teorii plazmy" [Problems of Plasma Theory], Moscow, Vol 4, 1964; R. Z. Sagdeev and A. A. Galeev, "Nonlinear Plasma Theory," Benjamin, New York, 1969; G. R. Ivanitskiy, V. I. Krinskiy and Ye. Ye. Sel'kov, "Mathematical Biophysics of Cells," Moscow, 1978.

4. Krinskiy, V. I., in "Problemy kibernetiki," Moscow, Vyp 20, 1968, pp 59-80.

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COLLECTION SUMMARIZES OCULOMOTOR FUNCTION RESEARCH

Moscow DVIZHENIYE GLAZ I ZRITEL'NOYE VOSPRIYATIYE (Eye Movement and Visual Perception) in Russian 1978 signed to press 25 Oct 78 pp 2-9, 276-277

[Annotation, Table of Contents, and Foreword from book edited by B. F. Lomov, Izdatel'stvo "Nauka", 3,650 copies, 278 pages]

[Text] Annotation

This monograph is devoted to today's most important problems concerning interaction of sensory and motor components of vision. It presents the techniques and basic results of original experimental studies.

The book is intended for physiologists, psychologists, and all who are interested in this problem.

Contents

Foreword, by B. F. Lomov

Systems analysis has now become the principal means of expanding and deepening our scientific knowledge. The more complex and multifaceted the phenomena under study become, the more acute becomes the need for applying the systems approach in their analysis. The human mind is a most complex and sophisticated form of expression of living nature's systemic properties. The multilevel hierarchical organization of mental phenomena demands an ability to constantly envision the mutual relationships of the different levels, irrespective of which of the sides of the mind is the focus of the researcher's attention. In this collective monograph, the dominant methods of scientific inquiry are represented by the most important principles of the systems approach.

The topical orientation of the book reflects a certain degree of consistency in the work being done by the Perception Process Laboratory of the USSR

Academy of Sciences' Institute of Psychology. The present monograph is a logical continuation of the previously published collection "Motornyye Komponenty zreniya" (The Motor Components of Vision) (Moscow, Izd-vo Nauka, 1975).

The visual perception problem has always been and continues to be one of the key problems in the overall structure of psychological science. This is entirely natural, since it is precisely in perceptual processes (among which vision plays the dominant role in relation to man) that we transform "the energy of external stimulation into a fact of consciousness."* We are well aware of the great significance attached to the formation of perceptual functions by the outstanding Soviet psychologist B. G. Anan'yev, who consistently defended the dialectical-materialistic thesis on the unity of the sensory and the logical in the human consciousness.

Effective work of sensory systems presupposes close interaction of the sensory and motor elements forming this system. The principle of "coordination of movement and sensation" was established by I. M. Sechenov back in the last century. The entire subsequent history of psychophysiology has confirmed the validity of this highly important principle many times, supporting it with new functional, morphological, and evolutionary data. In modern physiology of sensory systems, the concept of the unity of sensory and motor functions has become one of the fundamental principles.** The very title of the monograph presented here for the reader's inspection emphasizes that sensomotor interactions are the most important problem pertaining to the visual system.

Ideas developed in the book concerning the multilevel organization of the human visual system correlate with the results of research conducted by V. D. Glezer and L. I. Leushina at the Institute of Physiology imeni I. P. Pavlov--at the Laboratory of Vision Physiology, with the collective of which the authors and editors of this book have associated through scientific contacts for many years.

Internal and foreign scientific ties of the USSR Academy of Sciences Institute of Psychology were reflected within the overall structure and content of the monograph. Part Three presents the results of experimental studies performed by French and Czechoslovak colleagues in accordance with a program of joint scientific research, and studies conducted at the Tartu State University. Part Four contains clinical data obtained in one of the hospitals of Leningrad.

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* Lenin, V. I., "Poln. sobr. soch." (Complete Collected Works), Vol 18, p 46.
** "Fiziologiya sensornykh sistem" (Sensory System Physiology) (Edited by A. S. Batuyev, Leningrad, Izd-vo Meditsina, 1976).

The book begins with a section devoted to the early ontogenesis of oculomotor activity and the relationship this activity has with the development of some perceptual functions. Analysis of mental and psychophysiological phenomena as they develop is one of the main principles of the systems approach to modern psychological science. The psychogenetic aspect of the research helped us to reveal the basic levels in the highly complex hierarchy of mental processes, and to determine the way these levels interact and the dynamics behind supercession of the determinants of development.

According to Piaget's conception mental functions begin to take shape in a child's ontogenesis at the stage of its sensomoter development. The role of visual sensomotor coordination in this highly important stage of psychological development avoided the awareness of researchers for a long period of time, mainly due to the methodological complexities of recording eye movements. Application of objective methods of recording oculomotor reactions in newborn children and infants demonstrated that motor coordinations develop in the visual system significantly earlier than in other muscular somatic systems.

Parallel study of the sensory functions of vision (in which eye movements were often interpreted as an indicator of discrimination of objects and their properties by a child) persuaded researchers that an infant's visual world is incomparably richer and more complex than had been presupposed a few decades ago. It has been revealed as an example that the capability for distinguishing the principal three-dimensional characteristics of the environment takes form prior to purposeful movements of the hands and locomotor acts, and that it is apparently associated with development of sensomotor coordinations.

The research contained in Part One is a direct continuation of previous work published in the book "Problemy geneticheskoy psikhofiziologii cheloveka" (The Problems of Human Genetic Psychophysiology) (Moscow, Izd-vo Nauka, 1978). The principal results of the previous work served as the starting point for the experimental tasks reflected in the present publication. The main accent was placed in this case on deepening our explorations in those directions where information was either absent altogether or was clearly contradictory. The experiments described below were aimed at: a) analyzing the dynamic characteristics of eye jerks (saccadic movements) viewed as the most important element of oculomotor activity, b) studying the structure of the field of vision and the influence of this structure on organization of eye movements, c) obtaining and analyzing facts concerning vergent and cooperative eye movements, d) obtaining and analyzing facts on the specific features of optokinetic nystagmus in infants. The results of experimental research permit us to fill in certain gaps in our knowledge concerning the early ontogenesis of oculomotor functions. They imply very early development of intersensory (vestibulo-ocular) interactions in the child, something that B. G. Anan'yev indicated many times in the general theoretical aspect. This research was

used as the basis for an attempt to associate the unique features of a child's eye movements with the dynamics of the development of the peripheral and cerebral structures of the visual system.

Analysis of sensomotor interactions proceeding in the human visual system requires the use of special methods combining high precision with sufficient flexibility and universality. Such requirements are satisfied by the method of optical transformation of visual feedback, which permits us to easily change spatial relationships within the field of vision and broadly vary the feedback coefficients in the visual system in relation to both monocular and binocular vision. The experimental results acquired with the use of this method are presented in Part Two.

The analysis performed by the authors on the basis of extensive facts affords a possibility for revelaing the qualitative and quantitative dependence of eye motor functions on the magnitude of visual feedback and the specific features of the visual tasks. The diversity of forms of oculomotor activity accompanying feedback transformation and the close mutual relationship existing between the visual and vestibular systems are demonstrated.

Affording broad possibilities for analyzing sensomotor interactions within the visual system and the relationship the visual system has with other body systems, the method of optical transformation of visual feedback may be interpreted as a concrete form of systems analysis. The principal results of this phase of the research permit us to formulate a general idea about the oculomotor system as a tracking system with variable parameters, to isolate the principal mechanisms behind regulation of eye movements, and to define more specifically the influence of the functional field of vision on oculomotor activity.

Stability of the visible world occupies one of the central places within the complex of problems associated with analyzing the motor functions of vision. Movement of an image relative to the retina is elicited in some situations by movement of the object being observed and in others by movement of the eye of the observer. What mechanisms afford the possibility for differentiating between these situations? Several hypotheses have been suggested to answer this question, but not one of them has been confirmed conclusively. Part Three is a continuation of this long-going discussion. A critical examination of the existing points of view is combined in this section with an analysis of new experimental results obtained by the authors. New experimental data are used here as the basis for discussing the role of peripheral vision in the completion of tasks associated with determining the location of stimuli.

Eye motor functions are an inseparable component of all forms of cognitive activity interpreted as visual search. It is well known from clinical practice that many forms of mental disorders are accompanied by gross disturbances in cognitive motivation. Can we not utilize, in this connection, analysis of eye movements for diagnostic purposes? This is

precisely the way the question is posed in the final section of the monograph (Part Four). Relying on extensive clinical material, the authors tend to suggest that different mental deviations influence the nature of flicks (low amplitude eye jerks) in different ways. Flicks are interpreted in this case as a reduced form of eye scanning movements, and as an indicator of the activity of central mechanisms controlling eye movements. Study of flicks from these positions may promote further analysis of the multilevel systemic organization of cognitive processes.

Part One of this monograph was written colleages of the USSR Academy of Sciences Institute of Psychology--A. A. Mit'kin, Ye. V. Kozlova, Ye. A. Sergiyenko, and A. N. Yamshchikov; Part Two (1) was written by colleagues of the USSR Academy of Sciences Institute of Psychology--V. A. Barabanshchikov, V. I. Belopol'skiy, and N. Yu. Vergiles; Part Two (2) was written by V. I. Belopol'skiy; Part Two (3) was written by V. A. Barabanshchikov; Part Three (1) was written by V. I. Belopol'skiy, Part Three (2) was written by A. G. Luuk and M. Rauk (Tartu State University), Part Three (3) was written by V. Zikmund (Bratislava, Slovak Academy of Sciences Institute of Normal and Pathological Physiology), and Part Three (4) was written by Zh. Payyus, M. Shesna, and Zh. Leplya (Paris National Center for Scientific Research); Part Four was written by B. A. Karpov and A. N. Karpova (Leningrad, Hospital No 3).
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UDC 612.592.1+613.12(98)

PHYSIOLOGICAL AND HYGIENIC ASPECTS OF MAN'S ACCLIMATIZATION IN THE NORTH

Moscow FIZIOLOGOGIGIYENICHESKIYE ASPEKTY AKKLIMATIZATSII CHELOVEKA NA SEVERE in Russian by N. I. Bobrov, O. P. Lomov and V. P. Tikhomirov 1979 signed to press 28 April 1979, p 2, 3 - 4, 184

[Annotation, introduction and table of contents from monograph by N. I. Bobrov et al., Izdatel'stvo "Meditsina", 2,800 copies, 184 pages]

[Text] This monograph is the first generalization of contemporary concepts as to the mechanisms of the body's thermoregulation, the physiology of the sympatho-adrenal system and the reactivity of the human body in northern acclimatization. Providing the groundwork for the book are many years of personal observations by the authors who have employed up-to-date and complex physiological, biochemical and hygienic techniques of research aimed at studying the process of acclimatization together with principally new premises as well as extensive published material. The questions of thermal regulation by the human body in limited as well as in general chilling are treated in detail. The physiology of the sympatho-adrenal system and its effect on human metabolic process in the North are examined separately. The reactivity of a healthy body is discussed from the standpoint of studying the functional state of the adrenal cortex, circulatory system and general immunological response as well as the body's supply of vitamin C. Means for further study of human physiology and hygiene in the conditions of the North are noted as general biological problems associated with the various sectors of scientific and practical medicine. Techniques to facilitate the process of acclimatization to the severe climate conditions of the North are suggested.

This monograph is intended for physiologists, pathophysiologists, hygienists, biochemists and practicing physicians working in Northern regions.

The book contains 32 illustrations, 51 tables and a bibliography of 356 names.

Introduction

The 25th CPSU Congress has focused a great deal of attention on mastery of the vast natural resources and intense economic development of the northern regions of our country. In conjunction with this, studying the mechanisms of

human accomodation to the unique climate-geographic, industrial and social conditions of the arctic region has acquired an important significance.

In the medical and biological sense of the integral and interconditioned effect of a climatic complex, frequent aperiodic, sudden and drastic changes in meteorological factors are more discomforting for the human body than their absolute values and periodic changes [Danishevskiy, G. M., 1968]. Exaggeration of atmospheric phenomena and intensified cyclonic activity with sharp fluctuations in temperature and humidity, atmospheric pressure and wind speed over short intervals of time, the existance of the peculiar periods of arctic night and arctic day and cosmic and geomagnetic turbulence are characteristic of the polar climate [Alisov, B. P., 1969; Kuznetsov, S. A., 1970; Kaznacheyev, V. P., 1974].

The climate of the North which has been defined by a number of investigators as uncomfortable and severe [Arnol'di, I. A., 1972; Danishevskiy, G. M., 1968; Kandror, I. S., 1968; Kaznacheyev, V. P., 1978] or even "extreme" [Avtsyn, A. P., 1972] places increased demands on the human body, especially during the initial period of residence in the unfamiliar conditions of the external environment. Only a well-timed reordering of physiological functions to a different adaptational level can insure the possibility of man's worthwhile existance in new conditions [Frolov, V. M., 1972]. It is also necessary to bear in mind that the body's accomodation is achieved at the cost of a specified "biosocial price" [Avtsyn, A. P.; Marachev, A. G., 1975].

From the hygienic point of vew, the arctic climate is "irritating" (the criteria are severity and variability) as opposed to "soothing" or gentle and relatively constant [Danilova, N. A., 1971].

Lack of uniformity among the various microclimatic zones which are drastically different in terms of the pattern of meteorological factors is characteristic of the northern climate. Four variants stand out in the arctic climate: the Western mild, Eastern European, the Eastern Siberian continental and Far Eastern cold. It is believed [Alisov, B. P., 1969] that the basic factors forming the climate of some particular location are solar radiation, air circulation and the underlying surface. As a result of these climate producing factors, a unique physical and geographic environment is created in all four of the polar climate variants whose common features are a negative radiation balance, intensive cyclonic activity, general instability and variability in the weather, sharp fluctuations in meteorological factors and increased geomagnetic activity.

The difficulty of developing specific and nonspecific adaptive responses in humans coming to live in the northern regions ascribes a special scientific and practical meaning to human adaptation. As we know, adaptation is the ability to adjust to a changing external environment. The term "adaptation" is an extremely broad biological concept. In recent years, a number of authors [Deryapa, N. R., Ryabinin, I. F., 1977; Kaznacheyev, V. P., 1978] have proposed using only the word "adaptation" as a result of the preferred use of this term in international literature. In our opinion, in studies of

the body's adaptive responses to new climatic conditions, preference should continue to be given the term "acclimatization" as a particular form of adaptation. the concept of "climate" naturally infers the use of the term "acclimatization."

The primary object of this book is to present materials explaining some of the physiological and hygienic aspects of man's acclimatization to the North. It is primarily the result of research into thermoregulation which plays a leading role in the body's adjustment to low temperatures in the external environment. In addition, the questions of neural and hormonal regulation of physical functions, the properties of metabolism, saturation of the body with vitamin C and its immunobiological responsiveness are also explored. Morbidity which is an integral indicator of body condition in the conditions of a new climate is also discussed.

We have examined healthy young persons coming to the North from the central and southern portions of the country. Investigations were conducted during the initial period of acclimatization (six months to a year following arrival) as well as during the final stage of adjustment to the conditions of the arctic climate (2 - 3 years or more after arrival). This has made it possible to trace the dynamics of the physiological and biochemical indicators during the process of acclimatization and to discover the mechanisms of adaptational change to some extent.

The authors intend their work to be considered an appropriate contribution to the establishment of a new field of medical science — polar medicine and will conscientiously and gratefully acknowledge all remarks, advice and requests.

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THE 'POLAR STRESS SYNDROME' AND SOME PROBLEMS OF HUMAN ECOLOGY AT HIGH LATITUDES

Moscow VESTNIK AKADEMII NAUK SSSR in Russian No 1, 1980 pp 74-82

[Article by V. P. Kaznacheyev, academician of the USSR Academy of Medical Sciences, and V. Yu. Kulikov, candidate of medical sciences]

[Text] There has been an ever-increasing need to explore inaccessible parts of the earth in recent years, and to establish not only temporary, but permanent settlements there. Development of northern territories, in particular the north and north-east parts of our country is acquiring particular importance. Obviously, this cannot be done without bringing people there from other areas, and this makes a number of new biomedical problems particularly important. Among them, the study of processes of man's adaptation to both brief and long stays in northern regions is acquiring increasing practical significance. It is becoming increasingly apparent that it is important to develop, along with purely medical directions, those related to the study of ecological patterns and, in particular, those of human ecology.

In the latter case, we refer to a new interdisciplinary scientific direction, the patterns of interaction between man and the environment, dynamics of population growth, preservation of health, refinement of physical and mental capabilities of the homo sapiens species. We refer to demonstration of the patterns of interaction with the environment of large population groups which one arbitrary calls populations, by virtue of their socio-industrial, cultural and biological similarity.

Even now, we can single out some patterns for the populations of large territorial and industrial complexes, and some permanent settlements in the polar region, scientific stations in Antarctica and, finally, the population of the European and Asian north as a whole. In spite of the fact that such a distinction is arbitrary to some extent, the adopted approach makes it possible to study the most general and basic patterns of preservation and development of the health of man, with due consideration of the specifics of all climatogeographic and socioindustrial

conditions. Let us note that the concept of health of a particular man (individual) and the concept of health of a population are referable to different categories of research, even though they are interrelated and determine one another.

The health status of the individual can be defined as the process of preservation and development of his mental, physical and biological functions, his optimum fitness for work and social activity with maximum duration of active life. Health of a population is a process of sociohistoric development of psychophysiological and biological viability of the population, sociobiological succession of generations with ever increasing pace of national production, improvement of resistance of the population when exploring new territories or changing living conditions.

According to these definitions, along with criteria of health status of an individual, processing and generalization of which yield important information about the health of a population, we need some additional parameters that would reflect the status of a population as a single whole. One of the most effective means of obtaining such parameters could be to analyze anthropoecological patterns. Such studies are currently being developed and coordinated on the basis of the "Human adaptation" program, work on which is headed by the Siberian Branch of the USSR Academy of Medical Sciences and, in particular, the Institute of Clinical and Experimental Medicine.[1] More than 50 institutions of the USSR Academy of Sciences, USSR Academy of Medical Sciences, All-Union Agticultural Academy imeni Lenin, USSR and RSFSR ministries of health, other ministries and agencies are participating in research on this program.

In October 1978, the papers of Soviet scientists dealing with both clinical and anthropoecological directions of the "Human adaptation" program, delivered at the 4th International Symposium on Problems of Polar Medicine, in Novosibirsk, received a high rating.

"Polar Stress Syndrome"

The specific features of a number of diseases among indigenous residents and new arrivals to northern territories have been demonstrated rather well in the medical literature. Let us discuss some of them. According to the data of the Institute of Geography of Siberia and the Far East, Siberian Branch of the USSR Academy of Sciences, there is a rise in morbidity rate among immigrants from other parts of the country as the geographic contrast increases. For example, among settlers in Kamchatka, the morbidity rate is 9.6 times higher for those who came from Transcaucasia than from northern regions, it is 4 times higher for those from Kazakhstan and 3.2 times higher for those who arrived from the central zone of Russia.

It is not only the morbidity rate as a whole, but the structure of morbidity in the Extreme North, among both new arrivals and indigenous population, that differ from that of the central zone. There has been an appreciable rise in incidence of myocardial infarction in, for example, Arkhangel'sk, in the last few years, and the disease usually occurs in atypical forms that are difficult to diagnose.[2] Analogous findings have been made in certain urbanized regions of the northern Asian part of the USSR and several Scandinavian countries.[3] As a rule, serious forms and frequent complications of cardiac ischemia are encountered among new arrivals. Ischemic heart disease is encountered among the rural population of, for example, Yakutia, mainly among individuals over 60 years of age, and it has a relatively mild course. Studies of morphogenesis of coronary atherosclerosis revealed that stenotic lesions to coronary arteries occur 20 years later and 4.6 times less often among Yakuts than in nonindigenous inhabitants.[4]

Inflammatory lung diseases hold a prominent place in the structure of morbidity of new arrivals to the Extreme North. Comprehensive studies of pulmonary hemodynamics of healthy adapted males who had lived for 3-5 years in northeastern USSR revealed a significant change in pulmonary circulation on the organic, tissular and ultrastructural levels.[5] The aggregate of such changes in the lungs, observed in essentially healthy individuals adapted to several regions of the Extreme North, which were the result of man's exposure to different ecological factors, was named "Magadan pneumopathy" by A. P. Avtsyn. Evidently, these changes in the system of respiratory organs can explain the drastic prevalence of mortality due to pneumonia among adult male new settlers in Yakutia (16.2%), as compared to the indigenous population of the north (3.4%). On the whole, the death rate due to pneumonia is 1.5 times higher in Yakutsk than in the Moscow suburbs [Podmoskov'ye].[6]

Thus, the enitre diveristy of clinical manifestations of various pathological processes in the Extreme North is attributable to the effect on man of the set of ecological factors (climate, biosocial rhythms, endemic infections, nutritional distinctions, etc.) that exert their influence on different levels of organization of living beings. Changes in regulatory and homeostatic systems, which arise as a result of these factors, directly precede onset of pathology, determine its nature and specifics. For this reason, consideration of early signs, not only of disease but premorbid states, i.e., determination of the degree of fatigue of the organism, serves as a mandatory stage of studies directed toward elaboration of criteria of reliability of the biosystem when exposed to extreme and subextreme factors, for developing adequate methods of correcting and treating the observed disturbances. In essence, the degree of adaptive stress of each individual could serve as the basis for so-called prenosological (premorbid) diagnostics, while the indices of adaptive stress of a population should become the basis for organizing a universal prenosological dispensary service for the public and elaboration of more effective life support systems for a given population in each concrete region, on the basis of the obtained data.

A logical question arises: Do we presently have the necessary data to try to demonstrate some specific features in the change in health status of people who travel to and work at high latitutes? The answer to this question is of basic importance, since it pertains to research pursued under different extreme conditions: high altitudes, deserts, space, etc. We refer to the need to develop a distinctive classification system that would reflect the degree of stress and specifics of adaptive processes and health of people, which are inherent in various climate-geographic and socioindustrial conditions as a whole, and regions of the Extreme North in particular.

We have expounded the hypothesis that the specific form of chronic stress that occurs in man in the Extreme North, which is induced by an entire set of physical, biological psychophysiological and other exogenous ecological factors, could be called the "syndrome of polar stress."[7] The presence of this "syndrome" does not yet indicate a pathological process; it merely characterizes the specificity of the adaptation process, its systemic nature and close correlation to the structure of active ecological factors. Singling out this concept at the present stage of research is related to the need to demonstrate the most common and unique elements of metabolic and behavioral reactions that could restrict the adaptation process in the Extreme North.

One of these reactions is the moderate increase in 11-oxyketosteroids and total lipid content in the blood of new settlers; the latter is closely correlated with changes in concentration of total fraction of low and very low density lipoproteins. These parameters are indicative of the increasing role of lipids in energy metabolism during man's adaptation to high-latitutde factors, and they are associated with changes in other types of metabolism, in particular that of carbohydrates, proteins, vitamins and trace elements.[8] The increase in role of lipid metabolism in supplying energy for adaptive reactions is attributable to the fact that the shortage of water-soluble vitamins, such as B_1, B_2 and others, in the north is not associated with the typical signs of hypovitaminosis. One can only judge the shortage of water-soluble vitamins in the north on the basis of biochemical changes characterizing deadaptation changes in carbohydrate and lipid metabolism, which are manifested by the change of energy metabolism from the "carbohydrate" type to the "fat" type. In the presence of chronic stress when, as we have indicated above, the role of lipid metabolism increases in supplying energy to the body, real prerequisites are produced for oxidation of lipids via the free-radical route, rather than the enzymatic, with formation in tissues of toxic products--hydroperoxides of fatty acids, free radicals, aldehydes, epoxides, etc.[9]

A set of enzymatic and nonenzymatic antioxidants is used to protect tissues against development of free-radical oxidation of lipids. This set includes

a number of lipid-soluble vitamins, in particular vitamins E and A, the requirement of which should, of course, increase in the case of intensification of lipid metabolism. A decrease in tocopherol and carotene content was demonstrated in essentially healthy people in the polar region, as compared to a group from the central zone. As we have shown previously,[10] these changes are associated with increased oxidizability of lipids of biological membranes (in particular, erythrocytes) via a free-radical mechanism, and a change in oxidative processes in body tissues as a whole. On the basis of existing data on the role of fat-soluble vitamins in regulation of physicochemical properties of biological membranes and tissular metabolism, it can be assumed that the changes in various types of metabolism, in particular lipid metabolism, observed among new settlers of the north may be one of the prime factors determining the distinctions of adaptive reactions and human pathology at high latitutdes. Works published aborad concerning the role of fat-soluble vitamins and lipid peroxides in the pathogenesis of heart disease (in particular, cardiac ischemia) and cerebrovascular disorders confirm the thesis we have advanced.

Thus, the set of ecological factors of the Extreme North (psychoemotional stress, biorhythms, climate, electromagnetic fluctuations, specifics of work, living conditions and others), which affects man via different mechanisms, some of which are discussed here, appear to be integrated on the level of biological membranes, by means of modification of their properties due to a change in quantity and quality of lipids, concentration of fat-soluble vitamins, lipid hydroperoxides, etc.

Let us stress that the different psychophysiological changes that are observed among residents of the north at different times after they arrive there--temporary sleep disorders, asthenization, neurotic manifestations, so-called "polar" dyspnea and fatigability--are apparently based on similar biophysical and biochemical changes on the level of cellular structures. These changes subsequently become the primary basis of various individual manifestations of adaptive stress, prepathological and pathological states. In essence, we are dealing with a special state of the body, characterized by specific changes in deep-lying processes of cellular metabolism. According to our data, heliogeomagnetic fluctuations are of special significance here in the spectrum of ecological factors.[11]

As we have already stated, the presence in man of the "polar stress syndrome" does not signify a pathological state, but defines the distinctions of the process of adaptation and possible outcome of diseases. A prolonged state of stress may end (most often with proper medical screening, adherence to the necessary hygienic regimen for work and rest) with a state of adaptation, preservation and development of health. In some people, it could end by having homeostatic systems move to a new thermodynamic level at a certain "biosocial cost," as expressed by a change in health status, life span, reproductive distinctions, change to some form

of pathology, which is usually characterized by a chronic process. There may also be exacerbation of prior diseases.

The proposed conception has already enabled scientists at the Siberian Branch of the USSR Academy of Medical Sciences to recommend a set of measures to correct and prevent deadaptation states and a number of pathological processes that are the most significant for regions of the Extreme North. These recommendations propose the use of special "antistress" diets, wide use of antioxidants and agents that enhance their action in the treatment of chronic pneumonia, peptic ulcers, etc., rational organization of watch duty, expeditions and schedule for work and rest. It is growing more and more apparent that the diversity of natural-climatic, industrial and social conditions in the northern and northeastern parts of our country, where major special-purpose programs are presently being implemented, makes it imperative to refine scientifically substantiated forms of organization of work, life and recreation for groups of people differing in genetic, professional and social respects. Even now, for example, some quite encouraging results have been obtained with respect to refinement of the system of life support in Noril'sk and at its combine, which is directed toward increasing the effectiveness of processes of restoring health, early detection and prevention of diseases. It can be stated that we are coming close to organizing a "health industry," i.e., scientifically substantiated control of the health status of both the individual and population as a whole.

Some Distinctions and Prospects of Studying Human Ecology in the Extreme North

Academician S. S. Shvarts, who singled out three main sections in modern human ecology--factorial and population ecology, as well as biogeocenology--stressed that the first two sections are being studied the most comprehensively and effectively by special disciplines (medicine, physiology, sociology, genetics, etc.), i.e., in this case we are dealing in essence with introduction of ecological thinking into theory and practice of these studies. In the opinion of S. S. Shvarts, human ecology as an independent interdisciplinary direction should have as its goal the elaboration of principles for organization of a unified economic-geographic region, and such work must be based on the study and interpretation of technicoeconomic prerequisites, and they should end with advancement to a new and higher level in economics, creation of a general scheme for development of a region and biogeocenotic surface of earth.[12] In our times, the anthropobiogeocenotic aspect, development of effective criteria for making evaluations of health status and long-term forecasts for the health status of large population groups.

The ever increasing pace of scientific and technological progress leads to the situation where human society is becoming, in the words of V. I. Vernadskiy, "the only agent of its kind in the biosphere whose power grows with the passage of time with every increasing speed. It alone

alters the structure of the very foundations of the biosphere."[13] At the present time, we are witnessing such a process, and it is global in nature. We are observing the formation of a noosphere, a certain phase of development of the surface of our planet, when all of its geological, climatic, energy and other resources and capabilities are being wisely transformed into an integral system. The role of research on human ecology during this period of formation of the noosphere--noospherogenesis--is increasing substantially, since it is growing more and more apparent that the health status of the people is the most important reserve for labor resources when there is a quantitative shortage thereof, both in the country as a whole and regions of the Extreme North in particular. We can mention a number of biomedical and social distinctions of the inhabitants of northern regions, which distinguish their ecology from the ecology of inhabitants of other parts of our country and thereby reflect the specifics of formation of the noosphere in these territories.

In the first place, development of northern and northeastern regions of our country is being performed with the use of high-power energy resources, by means of implementing major national economic and scientific special-purpose programs. And man has to live in an artificial, "technologized" environment.

In the second place, our times are characterized by the increasing involvement of different groups of people in migratory processes. On the one hand, migration of large groups of people of all ages and specialties serves as the effect and, on the other hand, one of the main moving forces of scientific and technological progress. At the present time, there remain fewer and fewer of the customary populations all over our country and especially in the Extreme North who live permanently and work in their customary ecological conditions. For example, the intensity of annual turnover of the inhabitants of the Noril'sk industrial region ranged in 1971-1975 from 25 to 30% of the figure for 1970. Overall arrivals there constituted 76% over the 5-year period and departures 62.3% of the 1970 level. According to the data of the sociological office of the Noril'sk Mining and Metallurgical Combine, up to 76% of hired employees were fired in 3 years. The existence of "flowing" populations, which exceed the objective requirements, is usually due to poor adjustment of new settlers, which is related to the effects of an entire set of causes. Among these causes, along with social, economic, communal and living conditions, changes in health status are holding a larger and larger place. Intensive migration processes also reflect the specifics of the psychophysiological set of new arrivals, determine some of the distinctions of domestic conditions, etc.

In the third place, a certain level of adaptive stress is inherent in both the individual and the population as a whole, which no doubt affects the course of infectious and noninfectious diseases.

In the fourth place, the adverse consequences of man's activities in the past extended primarily to specific objects in nature, and attention was focused on protection of the animal and plant kingdom, whereas today man himslef, his well-being and health are the target of the diverse consequences of interfering with nature.

The scientific and practical aspects of the above problems are acquiring international significance. Evidently, the need to develop polar territories of earth is an important stimulus for peaceful collaboration between many countries: the USSR, Finland, Sweden, Norway, Denmark, Iceland, United States and Canada.

In the light of the foregoing, several new problems arise, which are directly related to the subject of human ecology. We should discuss some of them in greater detail.

It is imperative not only to study health status, distinctions of pathology and degree of adaptive stress of a population, but on the basis of the obtained data, as we have already stated, to develop specific principles for organizing work and life, which would assure not only preservation of health, but development thereof, extension of the period of active life for the entire population of the Extreme North, against the background of the ever increasing pace of scientific and technological progress. It is imperative to develop criteria, taking into consideration the biomedical distinctions of the individual and population, that would define the adequate combination of intensity and duration of labor, both with the continued increase in size of permanent population, and with a certain share of those who work temporarily. This applies equally to major cities, industrial and transport complexes, and small temporary settlements, where work is organized by the duty shift--expedition method.

There must be continued in-depth research in the area of proper organization of so-called stationary bases (base cities and enterprises), from which organized worker groups should travel for temporary work at distant enterprises. For this, we need scientifically substantiated material on how to organize the system for restoring health (active and passive rest, vacation site, time for leaves of absence [vacations], etc.), distribution of consumer goods, etc. On the whole, the entire life support system for a given population and its recreational processes could be arbitrarily called a "health industry," whose main task is to reproduce the reserves of fitness for work, reproduction of the population itself with regard to quantity and quality.

Studies of the degree of adaptive change in individuals arriving in the Extreme North from different regions of our country have shown that the optimum solution is to organize industrial and economic facilities with identical technology, which would be situated mainly in the same time zone, both in the comfortable central climate zone and in the polar

region. This would make it possible to come close to scientifically substantiated planning to make up for the shortage of manpower in northern and northeastern regions of our country ("manpower [resources] bridge), with due consideration of biomedical distinctions and adaptive changes in new arrivals to the Extreme North.

Control of current processes of noospherogenesis, which can be done only under conditions of fully developed socialism, requires continued basic research of an interdisciplinary nature, in which human ecology should acquire increasing importance. Perhaps, the ingenious predictions of K. Marx will come true along this route; he stated that "in the future natural science will include the science about man to the same extent as the science of man will include natural science: it will be a single science."[14]

In conclusion, let us mention the most important facts and aspects of development of human ecology at polar latitutdes.

In the north, a high concentration of technology is taking place; development of the territory is proceeding at an exceptional pace along the order of a "technogenic explosion." In previously virtually uninhabited regions, large territorial industrial complexes are being formed; colossal natural and manpower resources are becoming involved in the economic revolution [turnover?]. In the past few years, the volume of freight transported over the northern sea lanes has increased by several times. There has been an increase in amount of oil and gas recovered; exploration of new deposits is expanding continuously. Rational, "noogenic" control of this explosive process, which is taking place under the conditions of specific northern ecosystems, requires in-depth investigation of the patterns of interaction between biospherogenesis and noospherogenesis, on the one hand, and technospherogenesis, on the other.

The processes of man's adaptation to the north, which are not stationary and transitory in nature, are profoundly specific ("polar stress syndrome"). They present a complex combination of biological, social and technical components. Under such conditions, such a mechanism of biosocial adaptation of man as migrations acquires special significance. Against the general high migratory mobility of the nation's population toward eastern and northern territories, it increases by 3-4 times, "draining" 15-20% or more annually of the population of a number of industrial centers. A distinctive type of "flowing" population is formed, the composition of which changes continuously, with retention and even increase in volume. Under such conditions, many traditional therapeutic and preventive criteria and standards turn out not to be effective enough, since they do not take into consideration processes of biosocial selection, of permanent renewal of the population. There is a qualitative change in content of such concepts as "habitat [living environment]," "regional physiological norm," etc. The ecological approach requires development

of the typology of states of the natural and industrial environment and states of the organism and population, as biosocial systems that would conform with them; methods must be developed to evaluate the ecological and geographic contrast when there are interregional migrations; anthropo-ecological atlases of the SSR must be charted for rational organization of migratory flows. It is imperative to elaborate the dynamic aspects of human ecology and to correct, on this basis, the principles of modern balneology, formation of recreational systems and planning of migrations.

The specifics of function of controlling and homeostatic systems of the body under normal conditions and in a state of acute or chronic stress and pathology are ecologically determined. This must be borne in mind when developing principles of regional occupational screening, vocational guidance, therapeutic and preventive measures.

Since the health of the people under developed socialism must be viewed as a systemic, multifunctional concept, the content of which is far from being limited to traditional medical categories and includes social, economic and other components, we are developing structural and quantitative approaches to the "measurement" of health as an integral criterion of the effectiveness of life support systems for man.

More and more apparent here are tendencies to alter the type of interaction between man and nature, the change from the heterotrophic phase of utilization of nature to the autotrophic one (V. I. Vernadskiy). Being essentially an element of noospherogenesis, these trends are particularly important in solving problems of ecological economic planning in the north, taking into consideration the objectives of preserving and wisely changing natural ecosystems. In this respect, there must be development of advance "macrobionic" principles for organizing the technosphere, which would provide for closed chains of exchange in the cycle of "society--industry--nature--industry--society," which would make it possible to provide for adequate interaction between the technosphere and biosphere. In this category of tasks, an appropriate place should be found for development of the means of aerospace monitoring [control] of natural and anthropogenic ecosystems, bioengineering control of large fragments of the biosphere in the interests of society.

Finally, a blend of studies of dynamic processes of noospherogenesis and noocosmogenesis should constitute an important aspect of human ecology. In our opinion, comparing processes of development of the extreme territories on earth with such processes in space is not only and not so much a metaphor as a deep and constructive hypothesis that merits special methodological development. When preparing and approving major national economic plans, it is imperative to organize not only ecological but anthropoecological expertise. The development of highly efficient life support engineering systems for both individual and collective use, maximum increase in their reliability, studies of the distinctive

psychophysiological, psychological and psychosocial functions of man, the specifics of correlations between macroecological and microecological levels and the particular susceptibility of polar regions to cosmic factors--all this constitutes a far from complete list of the aspects of this interesting and important problem.

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V. HUMAN FACTORS

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PSYCHOLOGY AND THE PROBLEM OF RELIABILITY OF THE RAILROAD ENGINEER

Moscow INZHENERNAYA PSIKHOLOGIYA I PROBLEMA NADEZHNOSTI MASHINISTA in Russian 1978 signed to press 25 Aug 78, pp 4, 5-8, 238-239

/Annotation, Foreword, Introduction and Table of Contents from book by L.S. Nersesyan and O.A. Konopkin, Moscow "Transport" 1978, 239 pp, Foreword by Doctor of Medical Sciences, Professor F.D. Gorbov/

/Text/ This book presents an analysis of psychological aspects of reliability of performance of railroad locomotive engineers. It presents considerations of medical-biological and psychological factors which affect the engineers' performance, psychological and engineering optimization of monitoring and control of the locomotive, methods of selecting persons to work as locomotive engineers and basic occupational qualities required and factors involved in the formation of driving habits. It also describes peculiarities of the work of the locomotive engineer in an "autoengineer" system.

The book is intended for the use of designers of automatic control systems and may also prove to be useful to psychologists, psychophysiologists and engineers involved in problems of the scientific organization of labor. It will also be of interest to locomotive engineers.
16 illustrations, 21 tables, 74 references

Foreword

At present, when, literally complying with the law of inertia, we still hear debates about the subject of psychology, many of its sectors already are firmly entrenched in both its subject matter and in its research method.

For example, the latest achievements of educational psychology are connected with the demands of life, introduced by the scientific and technical revolution and problems of the socialist construction. We can say the

same about such specialized areas of psychology as engineering psychology, aviation psychology, space psychology and railroad psychology.

In the last several years, railroad psychology has not only become an independent science but also has achieved significant successes. We may say, without exaggeration, that railroad psychology occupies an important place among the scientific and practical sectors of psychology and especially in engineering psychology. This, of course, has its own causes.

First, the timeliness of all trends of research. The vast importance of railroad transportation for the socialist construction. The degree to which it is increasing in our day can be demonstrated merely by mentioning construction of the Baykal-Amur trunk line.

Second, are problems associated with the duties of railroad transportation workers. In this case, the duties of one of the central occupations, that is, engineers who operate modern mainline locomotives.

Of course, the importance of the outstanding problems does not, by itself, make a study valuable. However, railroad psychology, as an independent sector of knowledge, may be given the highest evaluation since it determines its own object of study and develops its own methods and approaches to the study.

The main thesis of the authors is the proposition concerning the dynamism of transportation situations, concerning the control of a powerful moving object, concerning the great cost of error. It is not surprising that a basic purpose of the book is the study of the reliability of the engineer, including conditions and measures for increasing this reliability. It is natural that such a generalized concept as reliability required attention to the most diverse aspects of the duties of the engineer, his selection and training and also to the "tools of his trade" on the engineering-psychological plane. The exposition of all of these problems is aimed at the solution of one main problem -- the problem of such rationalization of the work of the engineer by psychological means without which further significant increase of its effectiveness and reliability seems impossible.

The book contains both some important theoretical propositions and many specific practical instructions and recommendations. Both of these, stimulating the creative thought of practical transportation workers, have great value for the successful solution of man-related problems which arise in transportation.

On the whole, the book must be considered to be a great achievement. It develops and consolidates a new area of psychology -- railroad psychology. The value of the book lies not only in its use for operation of railroad transportation. The authors apparently were able to raise particular problems of the duties of locomotive engineers to the level of highly

serious generalizations and there is now a very wide audience of readers who are interested in these problems. However, the greatest value of the book lies in the personal contributions of the authors. It is an original work.

Introduction

The level of operation of railroad transportation, its economic effectiveness, the safety of freight and the lives of passengers -- all of these depend upon the performance of representatives of one of the largest occupations in railroad transportation, the mainline locomotive engineers. Among the sciences involved in the study of their work and contributions to its rationalization, an important place belongs to a sector of psychological science -- railroad psychology.

Railroad psychology is a specialized area of psychology utilized in the solution of a wide range of technical problems of railroad transportation from the point of view of principles of human work activities.

The practical importance of railroad psychology increases in proportion to the level of technical equipment of transportation, to the increase of speed of trains, to the introduction of autotelemechanical monitoring and control. It is precisely this increasing importance of psychological science which makes vital the systematic exposition of results of psychological studies conducted by railroad transportation psychologists.

Control of a fast-moving object, the dynamism of transportation situations, the great demands for thoughtfulness of the operator (especially the solution of operational problems in a short period of time), the constant readiness for emergency action within a long, monotonous period, the great personal responsibility and many other factors determine those specific features of occupational duties in railroad transportation, the study and evaluation of which, as factors affecting the successfulness of performance of duties and, equally, as the means of determining some measures of improving the reliability of performance of the engineer, is unthinkable without special psychological competence.

This book also presents an exposition of problems of railroad psychology, as methods of studying performance, primarily in a systematic functional approach to psychological analysis of work, optimization of panel control indicators of locomotives, it touches upon problems of structural modelling of the occupational performance for formation of driving habits in emergency situations, it describes conditions of maintenance of vigilance and efficiency, processes of self-regulation of occupational performance and it proposes some methods of occupational selection of candidates for work as mainline locomotive engineers.

The practical orientation of the book could not disregard the necessity of exposition of some fundamental problems which at present cannot be considered to be decisive in theoretical psychology and the physiology of labor. These include: development of methods of occupational selection, study of regularities of the dynamics of readiness for emergency action, a systematic-functional approach to solution of problems of evaluation of occupational reliability, experimental modelling of mechanisms of self-regulation of occupational performance, etc..

At present, industry and transportation of our country, fulfilling decrees of the 25th CPSU Congress, are persistently solving the problem of further increase of labor productivity. The solution of this question is connected with the search for and use of supplemental resources. They may be revealed by the use of scientifically based organization of the labor of persons working in modern technical control systems.

A scientifically based organization of a "man-machine" system is impossible without the use of the achievements of both general psychology and specific engineering psychology and the psychology of labor, which are accumulating considerable amounts of scientific knowledge which may and should be used in real practice to increase the effectiveness and reliability of human performance. This is even more necessary in view of the fact that, with the increase of speed and poser of transportation systems, the importance of "human factors" in the development and use of new forms of technology is increasing even more.

The railroad engineer's occupation is becoming more complex and the organizers of the occupation are now facing and will continue to face ever new problems of judicious and precise coordination of the characteristics of the machine with the psychophysiological peculiarities of the human being.

This book presents an exposition of many years of study of the occupational performance of mainline locomotive engineers. The authors hope that their modest contribution will facilitate the increase of labor productivity of railroad transportation workers and the increase of safety of movement of trains.

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EFFECTS OF EMOTIONS ON CARDIOVASCULAR ACTIVITY

Moscow EMOTSIOGENNYYE STRUKTURY MOZGA I SERDTSE (The Brain's Emotiogenic Structures and the Heart) in Russian 1979 signed to press 12 Jul 79 pp 2-8, 93

[Annotation, Table of Contents, and Introduction from book by I. I. Vaynshteyn and P. V. Simonov, Izdatel'stvo "Nauka," 2,850 copies, 93 pages]

[Text] Annotation This monograph is devoted to the results of experimental research on the activity of the normal and the pathologically altered heart of dogs and rats subjected to direct electric stimulation of the brain's emotiogenic structures. Cerebral mechanisms responsible for emotional states are analyzed in light of the "information theory of emotions" proposed by P. V. Simonov. The authors conclude that all intensely proceeding emotions are harmless to the healthy heart. In the event that cardiac pathology exists, passive avoidance and asthenic-depressive states, together with the parasympathetic effects typical of them, have the most unfavorable influence. Theoretical analysis of their experiments and the published literature permitted the authors to formulate a number of principles concerning psychological prevention of the harmful influence of emotions upon the human cardiovascular system. The book is intended for a broad range of specialists--physiologists, psychologists, and clinical physicians.

Four tables, 32 figures, 150 bibliographic references.

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Introduction

> Physiology teaches us--more fully and perfectly with time--how right--that is, how useful and pleasant--it is to work, rest, eat, and so on. But this is not all. It teaches us how to correctly think, feel, and desire.*
>
> I. P. Pavlov

There is an obvious gap between the persistent references by clinical experts to the influence of emotions upon cardiac activity and to the role emotions play in the origin of cardiovascular diseases, and the precise physiological data available on the laws, mechanisms, and paths of such influences. Beyond the fact that this problem is extremely complex, there are objective difficulties in experimental study of this problem, inasmuch as, in the opinion of many researchers, we are basically deprived of the possibility for appraising the emotions of even the highest mammals.

The verbal report of a subject concerning his state continues to be the most dependable information in research on human emotions. This is valid also in relation to another effective method of research on the cerebral mechanisms of emotions--direct stimulation of cerebral structures by electric current through preimplanted electrodes. V. M. Smirnov (1976) has presented the fullest summary of data obtained by means of therapeutic and diagnostic stimulation.

Summarizing the results of his own observations and information gleaned from the literature, V. M. Smirnov notes that when nuclei of the amygdala are stimulated, the patient reports arisal of fear, anger, and rage, and rarely pleasure. Stimulation of the septum, on the other hand, is accompanied as a rule by euphoria, satisfaction, sexual arousal, and general elevation of mood. When the anterior and posterior divisions of the hypothalamus are

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* Pavlov, I. P., in "XV Mezhdunarodnyy fiziologicheskiy kongress" (15th International Physiological Congress), Moscow, 1936, p 139.

stimulated we observe anxiety and rage, while when structures of the midbrain are stimulated the emotions assume a broad spectrum from anger and tension to sexual arousal coupled with a pronounced positive element. In contrast to the situation with the cerebral formations listed here, stimulation of the hippocampus is not accompanied by fear, rage, or pleasure. The only reactions that have been recorded include confused consciousness, temporary loss of contact with the physician and, on occasion, fear taking the form of the subject's secondary emotional reaction to disturbed perception of the surrounding world. When the mesencephalic division of the stem and the nonspecific thalamus are stimulated, a state of heightened activation or inactiviation arises. The activated states have a positive emotional hue, assuming an actively negative hue more rarely (rage, malice, but not melancholy and sorrow!). Inactivated states are typified by relaxation and indifference. Sensations of unusual "lightness of the body" or its "heaviness", arising in the presence of these two functional states, could not be directly associated with changes in muscle tone or vestibular functions.

In addition to the emotional states enumerated above, V. M. Smirnov's patients reported short-term reactions arising at the moment of electric stimulation:

a sense of confusion and bewilderment (mesencephalic division of brain stem, subthalamus, reticular thalamic nucleus);

fear, the cause of which is unclear to the subject or is associated with an emotional reaction to somatic changes (limbicoreticular system);

pleasure in the form of pleasant, not always accurately described sensations;

unmotivated joy arising upon stimulation of the medial nucleus of the thalamus, the globus pallidus, and the mesencephalic division of the brain stem.

In contrast to the situation with clinical physiological research, in which the physician maintains verbal contact with the patient, the experimental physiologist can appraise the emotions of an animal only on the basis of the external behavioral manifestations of these emotions. Once again we encounter an obstacle which is analyzed again and again in the works of A. V. Val'dman:

"When appraising the reactions of animals to electric stimulation of the brain, many experimenters oversimplify their appraisal and give their own interpretation to the essence of the animal's behavioral reaction. Most experimenters begin with the notion that an emotion is a form of behavior. If an animal cowers and runs away, they assume that this is a fear reaction, and if it attacks, they take this to be a reaction of rage" (Val'dman, 1972, page 13).

However, it has been demonstrated many times that both in natural conditions and under the influence of electric stimulation of the brain, we can observe a fully purposeful "cold-blooded" attack without objective indications of rage, a perfectly precise reaction of danger avoidance without fear symptoms, and ritual "warning" of an adversary (bristling fur, bared teeth, extended claws) without true anger.

A. V. Val'dman (1972) suggests distinguishing the following on the basis of his own systematic research:

emotional reactions--complexes of motor-autonomic manifestations devoid of purposefulness, typical of one emotion or another ("pseudoaffects," using the terminology of former authors);

emotional behavior--purposeful behavioral acts coupled with expressive signs of emotion;

an emotional state, which reveals itself only when the appropriate test objects are present in the environment (an experimenter, another animal, a danger signal, an so on).

An emotional state can be changed in animal experiments by weak (subthreshold) stimulation of cerebral formations which, when stimulated intensively, elicit emotional colored behavior. In A. V. Val'dman's opinion "it is precisely such states, and not the diverse manifestations arising in response to intense stimulation of these brain substrates, that can and must be qualified as the analogs of emotions in animals" (Val'dman, 1972, pp 22-23).

In his experiments aimed at revealing a latent "emotional state," A. V. Val'dman apparently activates that system (and not a single "point"!) of brain structures responsible for the given emotion. In the neurophysiological aspect we deal more often with the "emotional dominant" (as defined by A. A. Ukhtomskiy), which reveals itself upon additional activation by an external stimulus--a test object. These structures continue to participate in the regulation of an animal's purposeful activity and in enactment of "emotional behavior"; this is why we find it difficult to qualify only subthreshold "emotional states" as emotions.

While A. V. Val'dman feels it possible to interpret animal "emotional states" as analogs of human emotions, to include those arising in patients whose profound brain structures are stimulated (Ibid., p 22), the psychologist V. K. Vilyukas is more pessimistically disposed:

"The fact that the emotional sphere of mental reflection is absolutely inaccessible to direct study throughout the entire course of its biological evolution is a serious and, at first glance, an insurmountable obstacle hindering application of the evolution principle in research on emotional phenomena.... Even our judgements concerning the emotional experiences of

higher animals are, strictly speaking, only a hypothesis, an anthropomorphic projection based on a comparison of situations and behavior" (Vilyukas, 1976, p 35).

We cannot agree with V. K. Vilyukas' assertion. In our opinion the experimenter has a minimum of three possibilities for making objective judgements concerning the emotional state of an experimental animal.

The first of the indications we can employ is the presence or absence of autonomic changes and of typical alteration in brain bioelectric activity, on the condition that the physical load experienced by the animal and associated with performance of a motor act remains constant or decreases as adaptive actions undergo improvement. If the animal (and, to an equal degree, man) exercises the same motor habits while the autonomic and electrophysiological changes observed in the early stages of learning become increasingly weaker, we have substantial grounds for suggesting that the degree of emotional tension is gradually decreasing, since it is presently impossible to explain this phenomenon in any other way (Simonov, 1964; Preobrazhenskaya, 1969). P. Fress presents many examples of emotions weakening as adequate adaptive reactions undergo development (Fress, 1975, pp 133-134). Validly criticizing the hypothesis of so-called secondary motivations, according to which the fear emotion begins to substitute for a painful stimulus in the mechanism of conditioned reactions concerned with avoidance of pain, Zh. Nyutten writes: "...the compulsion to avoid a painful stimulus continues to operate (until such time that the animal realizes that the signal does not portend danger), but inasmuch as the animal experiences neither pain from the stimulus nor the threat of a dangerous situation, it does not manifest the more-emotional reaction of fear" (Fress, 1975, p 20).

But astounding facts indicating that the level of norepinephrine and serotonin decreases in both the brains of people ending their life by suicide in a depressed state and in the brains of animals (monkeys) in which depression is induced by zoosocial isolation attest to an obvious similarity of the neurophysiological substrates of emotions in man and animals. It would be difficult to compare the causes leading to chronic depression in an individual dissatisfied with his life and in a young monkey separated from its mother, but it does remain a fact that the same drug, the effectiveness of which stems from a similarity of the neurochemical mechanisms of depression, is capable of helping these two living beings.

The second indicator of an animal's emotional state may be the reaction of another individual of the same species to the signals of emotional expression of a partner, or the phenomenon of "emotional resonance" (Simonov, 1976, Val'dman, Kozlovskaya, 1976). This approach is one of the brilliant experimental findings of A. V. Val'dman and his laboratory, one which has fundamental significance to the general methodology of research on animal emotions. In distinction from a human observer, an animal is capable of detecting subtle nuances in a partner's emotional expression which slip by

an experimenter. Experiments conducted at Val'dman's laboratory showed that an animal observer sometimes remains entirely indifferent to obvious external manifestations of "rage" in a partner and instantaneously reacts to some sort of symptoms of a real threat unnoticed by the human eye. This approach is especially effective when the experimenter records, in the "detector" animal, not only the behavioral components of the reaction to the partner's emotional state but also the physiological changes occurring in autonomic functions, alteration of brain bioelectric activity, and so on.

But the decisive criterion for presence of an emotion in an animal, rather than some sort of other phenomenon of higher nervous activity, is, we are quite certain, the relationship the animal itself has to the state of its brain. What we are talking about here is the "hedonistic maximization-minimization principle."

"The nervous mechanisms of behavior are organized according to the hedonistic principle of maximizing positive arousal and minimizing negative arousal" (Young, 1967). It is precisely through direct stimulation of the brain by electric current that we are able to reveal, more so than with any other methodological approach, a positive emotional state which an animal tries to maximize--that is, intensify, lengthen, or repeat, or a negative emotional state which the animal (and, to an equal degree, man!) tries to minimize--that is, weaken, stop, prevent. We emphasize that an emotion should be identified in an animal not by the nature of an external factor (food may be repulsive to a sated subject while a destructive narcotic may elicit pleasure), but by the animal's active relationship to its state, as revealed in its behavior. It is precisely this behavior criterion and not expression taking the form of bared teeth, tail wagging, vocalizations, and so on that serves as the decisive indication, to the experimenter as to the absence or presence of an emotional state, and its positive or negative coloration. By subjecting the maximization-minimization principle to neurophysiological analysis we can clarify the role nervous mechanisms of emotions play in reinforcement of instrumental conditioned reflexes (Simonov, 1972, Wyrwicka, 1975, Cytawa, Trojniar, 1976).

Inasmuch as emotion is a direct reinforcement of instrumental conditioned reflexes, we believe that we can answer a question which has long absorbed the minds of philosophers, biologists, and psychologists: At what point in the evolution of the animal world on our planet did that form of reflection of reality which has come to be called "emotion" arise? If we follow the line of reasoning presented here, we would have to word the answer as follows: Those living beings which are capable of developing instrumental conditioned reflexes possess the nervous mechanism of emotions (or its phylogenetic analog).

And so, an animal's instrumental conditioned reaction to direct stimulation of its brain attests to the fact that we are dealing with the nervous substrate of positive or negative emotions, be the stimulus applied to emotogenic or some other brain structures. But the method of direct

stimulation is incapable of answering another question: Under the influence of what factors, with the help of what mechanisms, and with the participation of what sort of brain formations are emotogenic structures activated in the natural life of man and animals?

This is why, before proceeding to an analysis of the influences of the brain's emotogenic structures on the activity of the normal and pathologically altered heart, we must at least briefly dwell on the general physiology of emotions, with a consideration for the experimental data and theoretical conceptions our laboratory has accumulated in the last 15 years.
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VI. PSYCHOLOGY

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A NATIONAL PSYCHOLOGICAL SERVICE

Moscow VESTNIK AKADEMII NAUK SSSR in Russian No 1, 1980 pp 20-30

[Article by B. F. Lomov, corresponding member of the USSR Academy of Sciences]

[Text] The development of our society, humanization of all areas of social [national] production, scientific and technological progress have resulted in significant growth of a need for practical use of psychology in all areas of the national economy.

The inadequate use of practical psychology is particularly acute with regard to solving pressing problems: formation of the new man; education, upbringing and vocational guidance for young people; in the area of social and industrial management and production; design of new promising types of technology, creation and development of automated control systems, etc.

For development of applied psychology, as well as the solution of practical problems with use thereof, make it imperative, in the first place, to already deploy theoretical and scientific-practical research in the immediate future; in the second place, to make use of the knowledge gained in the actual endeavors of man. This means that the time is ripe to analyze and optimize the relations between theoretical and applied psychology, to develop effective ways and means of making use in practice of the results of psychological research.

Creation of a system of psychological service in our country will be a phase of paramount importance in applying psychology in the life and endeavors of society. Such a system would become the connecting link between science and practical use of its results. In the future, this should result in redistribution of the proportion of theoretical and practical projects, as well as functions of specialist psychologists: relative decrease in share of research work and increase in the role of applied psychologists in the area of operations, consultation, expertise, management, etc.

Analysis of the Soviet and foreign knowhow revealed that the use of already available psychological knowledge, for example in

designing and operating complex "man-machine" systems, makes it possible to increase substantially their efficiency, reliability and safety of operation. Formation of plans for social development of only one of the districts of Yaroslavl' with due consideration of sociopsychological data yielded an economic effect of over 8 million rubles, and introduction of psychological elements in rational organization of fishermen's labor aboard vessels of the Baltic fleet yielded one constituting 1.2 million rubles per year. In Moscow and Leningrad, where psychological studies are being pursued on a particularly broad scale, the volume of work done by economic contract with industry more than doubled in the past 5 years. All these facts reflect the increasing practical need to solve psychological problems, on the one hand, and indicate the maturity and fruitfulness of basic research, on the other.

It must be noted that both psychologists and specialists concerned with problems of man and practical application of knowledge gained to various areas of life of society are not yet always clearly aware of the need for broad use of the advances in psychology for continued socioeconomic development of our society, humanization of all areas of social life.

In spite of some positive changes (appearance of "embryos" of a future psychological service as a coordinated system of introduction, use and application of psychological knowledge), there are diverse interagency barriers; analysis and generalization of the knowhow gained in solving a number of practical problems has not been made deeply enough; practical requirements and their link with future directions of social and scientific-technological progress are not always taken into full consideration in selecting and developing many theoretical and scientific-practical problems. All this generates serious difficulties for the advancement of psychological knowledge over the theory--experiment--practice chain and, in turn, leads to some rift between basic and applied research in psychology, to shallowness of topics, duplication of projects, as well as impossibility of strategically planning basic research tied in with the cardinal problems of science and practical work.

All of the foregoing confirms the urgent need to build up scientific-practical psychology and organize a psychological service in our country.

The considerable experience gained in operating psychological services in some sister socialsit nations (GDR, Polish People's Republic, CSSR) is indicative of the national desirability and effectiveness of organizing such a service. Thus, according to data on operation of the service in CSSR, psychoprophylaxis and consultations in the areas of family, child education, early detection and prevention of "deviating behavior," and anomalous child development have made it possible to promptly detect and correct such deviations in about 30% of the difficult cases.

There too, work is being done in psychodiagnostics and professional screening in all of the main occupations involving increased responsibility or danger.

The experience gained in sister nations shows that many subdepartments of the psychological service (particularly its lower regional elements) are being run with success on a cost accounting basis.

In our country, concrete questions of organizing a psychological service became the subject of special analysis and consideration in 1978 at the Institute of Psychology, USSR Academy of Sciences, and USSR Society of Psychologists. They have been repeatedly discussed by the scientific council of that institute and at meetings of the central board of the Society. Several concrete suggestions were adopted, which will make it possible to complete in the very near future preparation of a comprehensive draft for organization of a psychological service in the USSR. It will contain suggestions on the structure of the service, its rights and duties, nature of interaction with other services, as well as questions of scientific and methodological supervision [control] and management of the service, organizational and financing, material and technical support of the service at different stages of its development.

* * *

Let us consider some forms of professional work of the psychological service, as well as standard problems that can be solved by it (with due consideration of Soviet and foreign knowhow and prospects of scientific and technological progress).

In the first place, this refers to diagnostic and prognostic work. This is directly related to problems of social, vocational, personality, individual diagnostics and prognostication. We have accumulated quite a bit of scientific and methodological knohow in this form of work. In the future, there must be broader deployment of studies, and the efforts of psychologists in different specialties must be concentrated on this.

In the second place, it refers to psychohygienic and consultant work. This includes psychoprophylaxis on different levels, vocational consultations in the broadest sense (medicopsychological and sociopsychological prophylaxis and consultations, industrial hygiene, vocational guidance and screening, correction of deviations, adaptation of the individual to a specific form of activity, etc.).

In the third place, it refers to work pertaining to setting norms and standards. This includes preparation of various regulations-related documents: methodological letters, recommendations, norms, sectorial and national standards, etc.

We have accumulated considerable experience (both positive and negative) in this form of activity, especially in the area of engineering and medical psychology. But, in essence, this is expereince in special application of psychological data to the solution of narrow aspects of practical endeavor--solution of special problems pertaining to the manufacture and use of some specific work tools and devices. Thus far, the problem of standardization of methods of psychological examination [or study] has not been sufficiently elaborated.

In the fourth place, this refers to expertise. This is the service of psychological expertise in different sectors of the national economy. Perhaps this is where we have gained particularly extensive knowhow and obtained the greatest results. This form of activity has already found practical applications in forensic, medical and engineering psychology, and in part in industrial psychology. However, standardized methodological and scientific bases have not yet been worked out for psychological expertise.

In the fifth place, this refers to designing. This special and quite promising form of work of psychologists, which is related to the development of complex and ultracomplex sociotechnological systems, emerged only in the last few years. Ultimately, most applications of engineering psychology should become one of the disciplines pertaining to design, since designing is related not only to the design of complex and ultracomplex systems, but the design of new and promising forms of human activity.

Implementation of psychological designing must begin with assimilation of the entire arsenal of professiographic methods (methods for psychological analysis of performance). Unfortunately, we still have not summarized the knowhow in psychological description of human performance, and for this reason we do not have reliable enough means for psychological evaluation thereof; we cannot choose scientifically substantiated ways and means of optimizing and planning both old and, particularly, new forms of professional activities.

In the sixth place, this refers to research. This form of work is not directly related to the psychological service, but is most intimately linked with it. It includes definition of problems, structure, prospects and the most important directions of scientific and practical research as related to the tasks for the psychological service, which arise in different sectors of the national economy. It also includes special scientific methodological work related to selection, verification, adaptation and introduction of the results of laboratory research to practice.

Of great importance is the question of areas of application of the future psychological service in the socioeconomic system of our society. Analysis and generalization of Soviet and foreign knowhow make it possible to single out these areas with sufficient certainty.

One of the main areas of future activity of the psychological service is production (including industry, agriculture, transport and communications). At the present time, there are various groups (and even institutes in some sectors) in some sectors that are concerned with work on problems of safety and scientific organization of labor; some special psychological laboratories have been opened, as well as centers for special planning of development of enterprises and sectors. But all of these scientific organizations are working without contact with one another.

> There is a rather ramified network of central and sectorial research organizations under the AUCCTU, which deal with problems of labor safety and analysis of work activity (a central institute and about 10 outlying ones with psychological departments). An independent network of such institutions has also been established under the USSR State Committee for Labor and Social Problems. In addition, each ministry has its own sectorial laboratories and laboratories at the head enterprises.

The second area of work for psychologists is education (from elementary school to the VUZ). At the present time, we have a network of institutions in our country that deal with questions of education: USSR Ministry of Education, USSR Ministry of Higher and Secondary Specialized Education, USSR State Committee for Vocational and Technical Education, Academy of Pedagogic Sciences and a system of departments of public education. Finally, there are the intermediate levels of the system of vocational training, a sort of transitional steps between the secondary school and industry; this is a widely branched but poorly organized network of institutions in the system of professional screening, training and consultation (for example, consultation offices at enterprises).

These institutions (which are also independent and separate) also create their own networks of psychological services that are not interrelated. As a result of such a situation, a standardized structure is lacking in the psychological service in the area of education, there is no general interpretation of its tasks and, accordingly, standardized [generally] performance thereof.

The third area of application refers to public health and medicine. It is perhaps here that the most systematized knowhow has been gained in applying psychology to specific practical activities. There is a ramified (in both structure and number) network of institutions under the USSR Ministry of Health, which are related to diagnostics and therapy of various mental disturbances, which employ medical psychologists. There are also major institutions of clinical medical psychology--psychiatric clinics, institutes of neurosurgery, clinics of organic pathology and mental diseases.

However, the psychologists working in this field are compelled to use mainly foreign (although significantly adapted [modified]) methods of diagnostics and analysis of pathological personality changes. For this reason, Soviet psychologists are faced with the acute task of working on methodological, theoretical and experimental-practical problems of psychology of the personality (not only its sociopsychological aspects, but general personality psychology). Hence, there are serious problems of general orientation and coordination of work, scientific substantiation thereof (we refer to the methodological and methodical system and means used to pursue practical [clinical] work).

The next area of application of psychological knowledge is forensic. This is a system that is related to jurisdiction, legal procedures and law, use and protection thereof. In recent years, some advances and prospects have emerged in this area of work: for quite a long time research has been pursued; the specific area of their practical application has been defined; the main objectives pertaining to future application of psychology in the area of law are more or less clear.

One of the most important problems is the study of abnormal, deviant behavior, normal and abnormal personality development and problems of social prophylaxis. Analysis and correction of psychology of criminals and delinquents, problems related to adaptation and readaptation thereof to social conditions are of great importance.

The fifth area of application of psychology is athletics. With each year there is expansion and partial implementation of the need for practicing psychologists to work with athletes (this applies, first of all, to the work of psychologists with sports teams and higher level sportsmen).

Thus far, sufficient experience has not been gained in the work of psychologists in the area of mass participation sports: there are no reliable psychological criteria and methods for screening prospective athletes; there are no scientific bases for evaluating the influence of mass scale [participation] sports on improving mental health and spiritual state of man.

There is an acute question of centralization and coordination of scientific and practical work in this area.

> In Moscow, two scientific research centers have been opened, one at the All-Union Scientific Research Institute of Physical Culture and the other at the State Central Institute of Physical Cutlure, where work is being conducted in the field of sports psychology. Similar work is being pursued on the chair of psychology (in sports) at the Leningrad Institute of Physical Culture imeni P. F. Lesgaft. But there is still no coordinated plan for interaction between researchers and practitioners, nor is there a standard [unified] work program for psychologists, even in scratch teams.

Increasing the defense capabilities of our country (military psychology) is another important area of practical application of psychology. In this area, we can single out several main directions. The first refers to psychological problems of moral and political indoctrination [education] of service men, where considerable practical knowhow has been gained, and there is a special scientific and practical center (Military Political Academy imeni V. I. Lenin). The second refers to problems of interaction between man and technology. We should mention the broad development of research pertaining to psychological and biomedical back-up of operator work, psychological expertise of technology (including new types of technology).

> Both directions are characterized by practical implementation of psychological knowledge: formulating the "nuclei" of the system of the psychological service, which are related to problems of professional screening, moral-political and psychological training, establishment of the bases for training specialists in the field of theory and practice of military psychology.

But, here too, there are unsolved problems related to coordination of work, standardization of diagnostic and research methods (for example, the ways and means of professional screening and training of specialists for diverse types of troops are still virtually unrelated to one another), development of a system for training and purposeful use of military specialists and military psychologists.

The seventh area of activity of the psychological service is art and cultural affairs. It is extremely difficult to discuss organization of a psychological service in this area. There is an entire set of problems that have not been worked on at all by psychological science, and they must be resolved for continued refinement of the strategy of cultural construction. In addition, the workers in the theater, motion pictures, television and music should be armed with deep enough knowledge about the fundamentals of psychology.

> Courses in psychology are given at Higher Directorial Classes, the GITIS [State Institute of Theatrical Art imeni A. V. Lunacharskiy] and at the Leningrad Institute of the Theater, Music and Cinematography; psychologists are working at most studios, and they deal with screening and training of actors, as well as help directors in their work. Special studies are being published in the field of musical education, as well as dealing with analysis of the sense of esthetics and psychological problems of perception of works of art.

At the same time, the psychological aspects of problems related to the increased need of society for further development of culture (as a means of mass communication, propaganda and mass education) and art (as a

specific area of human endeavor) are not being worked on deeply enough. A need has arisen for conducting major psychological research and practical implementation of acquired knowledge to practical refinement of this important area in the life of our society.

Science (as one of the most important areas of creative endeavor) is another poorly developed area of application of psychological knowledge. At the present time, scientific and practical research in the field of sociology of science is undergoing intensive development. In this regard, we shall have to determine whether it is desirable to introduce a psychological service in the area of science, as well as to determine the preparedness of psychological science to solve problems in this area.

At present, it is quite obvious that problems of activation of creative endeavors and the activities of creative teams have become one of the substantial problems, since science has acquired a mass scale nature and its role in the life of society is ever increasing.

Finally, the area of services is the last (but not in significance) area of activity of the psychological service. We should make a comprehensive study and analysis of foreign knowhow in this field (in particular, psychological analysis of advertising, demand and marketing conditions). In our country, such work amounts essentially to sociological interrogation and regulation of relations between producers and trade, between trade and consumers.

In view of the increase in leisure time, development of individual requirements, on the one hand, and increase in number of people working in the services area, on the other, we shall have to solve an enormous number of major theoretical and scientific-practical psychological problems in this area. Formation of requirements [demands] is one of the complex and pressing ones. Psychological science has only begun to work on it, and we are still far from a practical solution.

* * *

Establishment of a psychological service in our country is a rather complex and lengthy process. Psychologists are rather well aware of the main difficulties and problems that must be solved in the course of organizing such a service. They include the specifics of the territorial and demographic structure of the USSR (multinationality and regional differences in culture, traditions and life style), diversity and a certain dissociation of different areas of social practice, particularly industry--sectorial and departmental specifics thereof, a poor base, with respect to personnel, technology and methods, for establishment of a general national psychological service.

In this regard, there are plans to build a structure for the national psychological service that would branch out in several directions: regional centers and institutions; departmental, sectorial centers and institutions; scientific and methodological control [supervision] centers; management of the service along the lines of State agencies.

At the present time, at the first stage of establishing a psychological service, its main tasks are being defined in different areas of the national economy and social life of the nation's people, as well as standard [model] forms of work of practicing psychologists (consultations, planning [design] and operational, educational, expertise, preventive, etc.).

The exemplary structure of a national psychological service could be as follows.

A central council of the psychological service (CCPS), an agency of the USSR Council of Ministers at the head of the service (ranking either as one of the administrations of the USSR State Committee for Science and Technology, or an independent State committee).

The CCPS would have to be granted rights to define the research topics of applied psychological projects, distribution of allocations in different republics, publication of literature, as well as supervision of adherence to psychological norms in the nation's national economy and economic effect of psychological measures. It would implement centralized control of information gathering about the results of basic psychological research, as well as reporting the results of new projects to the lower-level organizations. The CCPS would administer the work of faculties of psychology and VUZ departments training psychologists (the number and specialization of students would be determined by the CCPS in agreement with the USSR Ministry of Higher and Specialized Secondary Education).

At first, the CCPS would be financed by the State budget and allowances [deductions] of ministries and agencies.

To perform its tasks, the CCPS will establish within its structure a coordinating council and information board, as well as (to administer various sectors of the psychological service) boards for engineering psychology, industrial psychology, social, pedagogic psychology and other psychological disciplines. The administrators of regional committees and their main departments, as well as prominent scientists of our country, will be called upon to work on the coordinating council.

The next hierarchic body of the psychologic service would be the regional committee (RCPS), which would combine the elements of the psychological service of several republics or large oblasts that are linked territorially, economically or scientifically.

The staff, financing and structure of the RCPS are analogous to those of the CCPS (except that departments will be organized in the RCPS instead of boards). The RCPS would perform the same functions within a region as the CCPS.

Municipal and rayon (rural) committees (MCPS, RRCPS) are subordinated to RCPS. The tasks of these bodies would include dissemination of psychological knowledge, control of the work of psychologists at enterprises and institutions, coordination of work wihtin a city or rayon, administration of operation of centers for vocational guidance and educational-methodological centers.

These bodies would be financed chiefly by allowances [deductions] from local enterprises and they would be staffed on the basis of combining permanent [regular] staff with individuals holding a job here along with another one elsewhere. The structure of these bodies would include a council, manned by representatives of enterprises and groups from social, engineering, general pedagogic psychology, industrial psychology and other psychological disciplines.

Pyschological service departments and groups would be the primary, bottom level departments of the service, working directly at enterprises, institutions and public education agencies (they would be on the budget of these organizations).

The structure of these primary departments of the service should conform with the specifics of a given enterprise and institution. Special groups, sectors (departments) of social and engineering psychology, as well as industrial psychology, will be established at each plant, in each scientific research institution and OKB [experimental design office, or special design office]. At each kolkhoz (sovkhoz), vocational and technical school, and school there should be working specialists in social and pedagogic psychology, and there should be specialists in industrial psychology at the educational centers and centers for vocational guidance. Engineering and social psychologists will be working as part of the Armed Forces. There are plans for permanent positions for medical psychologists in hospitals (clinics) and athletic schools (committees for physical culture and sports, sports societies). Special consultation centers should be established where all citizens of our country can consult social and medical psychologists. Specialists will deliver course at technical VUZ's on engineering psychology and industrial psychology, as well as psychological aspects of management in industry.

It must be stressed that the structure we propose here for a psychological service unquestionably requires additional polishing and testing. At the present time, suggestions of regional departments of the USSR Society of Psychologists are being considered at the Institute of Psychology, USSR Academy of Sciences.

Personnel training is one of the important aspects of organizing the USSR psychological service.

At the present time, we have nine scientific and educational centers in our country that train psychologists with higher education (about 500 people per year). The curriculum [syllabus] of these VUZ's is planned primarily for training future researchers or instructors in psychology. However, analysis of the distribution of graduated specialist psychologists (on the example of Leningrad University) revealed that the main demand (up to 80%) for psychologists stems from clinical [practicing] services, rather than research institutions. Most of the graduates, however, are not ready for practical work, and this leads to a low effectiveness of their work, their leaving the clinical area, changing specialty, etc.

The existing situation, as well as the tasks pertaining to establishment of a national psychological service, make it necessary to refine and partially alter the system of personnel training in the following directions: training of specialists for research and instruction work, training psychologists for practical work in medicine, in the field of upbringing, in industry and other sectors of the national economy; training of specialists in designing and operating complex "man-machine" systems (based at technical VUZ's); organization of psychological education for specialists in different sectors of the national econmy, in the system of higher education, medicine, culture, art, etc.; training and retraining of working psychologists; education and retraining in the field of psychology for specialists other than psychologists (engineers, pedagogues, physicians, administrative workers, etc.).

At the present time, at the initiative of the Institute of Psychology, USSR Academy of Sciences, and USSR Society of Psychologysts, an anlysis is in progress of the standard problems being resolved by clinical ["practicing"] psychologists, and a draft is being prepared of a "model specialist-psychologist." The experience gained in training graduate psychologists is being summed up by the USSR Ministry of Higher and Secondary Specialized Education and some of our country's universities (Moscow, Leningrad and Yaroslavl'); new curriculums are being prepared that are designed to training practicing psychologists.

It would be expedient to request in the immediate future that the USSR Ministry of Higher and Secondary Specialized Education consider the question of adding psychological disciplines to the curriculum of technical VUZ's (at first, one could establish special chairs of psychology at the leading technical VUZ's, as well as two or three chairs of engineering psychology in the nature of an experiment at the Leningrad Polytechnic Institute imeni M. I. Kalinin, Moscow Higher Technical School imeni N. E. Bauman, MAI [Moscow Aviation Institute] and Moscow Physicotechnical Institute). A draft curriculum and syllabuses for course in this field has already been prepared at the initiative of the Institute of Psychology and Moscow Higher Technical School imeni N. E. Bauman.

The equipment for psychological research [or studies] is an equally important issue.

At the present time, we are observing an appreciable growth in number and level of experimental and applied-experimental work in the field of theoretical and applied psychology. The results of such work are being used not only in theoretical research, but in practice. We refer to psychological diagnostics and prognostication of efficiency of man's work, evaluation and control of his state, evaluation of occupational screening and training, checking training of specialists, etc.

The wide practice of mass scale experimental and practical surveys raises the acute question of rational use of modern technology in psychological experiments, standardization of instruments and methods, expansion of nomenclature of equipment (ranging from unique laboratory equipment to portable units for mass-scale field studies).

> In our country, there are still no centralized, specialized services and enterprises for the manufacture of standard (mass scale) and research equipment. There are such firms in the GDR, Polish People's Republic, CSSR, as well as all major capitalist nations: Belgium, France, FRG, United States, Japan and others. In our country there are several enterprises and scientific research institutes within the system of the USSR Ministry of Health, that produce instruments for psychological research on a small scale, and they are not yet refined enough. The sectorial firms are only producing nonstandard equipment for the time being, either to meet the needs of a sector or orders of the USSR Ministry of Health.

In order to assure a reliable material and technical base for psychological research [studies] and the psychological service, it is imperative to establish an OKB for psychological instrument building, which should be asked to generalize and assimilate foreign knowhow, analyze information about instruments developed in our country, start developing mass scale and promising equipment for psychological research and examinations. The OKB should be supplied with an adequate production base, capable of manufacturing both small-series and standard, series-produced equipment for the psychological service.

* * *

At the first stage of deployment of a national psychological service, it would be desirable to establish a scientific council for problems of applied psychology (either under the Presidium of the USSR Academy of Sciences or Department of Philosophy and Law, USSR Academy of Sciences), for the control and management of this work, as well as scientific and methodological control in the future.

This scientific council should determine the most important needs of practice and first and foremost tasks for applied psychology; it should analyze and summarize the experience of applied research in different sectors of the national economy; it should check performance of such work; it should coordinate on a national scale the research done in the area of applied psychology and define the most important areas of practical application of psychological data; it should prepare a long-term program for development and implementation of applied psychological work (scientific-technological forecasts and goal-oriented programs); it should determine and coordinate the level and programs of basic research with the long-term practical objectives; it should allot manpower, equipment and material-technical resources to solve long-range problems; it should evaluate the effectiveness of solutions and check their implementation and use.

The first and foremost task for the scientific council will be to determine the structure and most important directions of applied psychology (for example, engineering, social, medical, pedagogic, industrial, educational, etc.), prepare programs for them and formulate prospective tasks. To do this work, sections and subcommissions will be formed within the scientific council to deal with the main directions of work, and they will consist of representatives of scientific and practical psychology, allied sciences about man and his labor, as well as representatives of consumers ["customers"].

The scientific council for problems of applied psychology will implement overall scientific-methodological and scientific-organizational supervision at the first stage of deployment of the USSR psychological service.

During this period, preparations will be in progress, at the center and in different regions, of the final draft for the USSR psychological service. The scientific council will coordinate and check work done to determine the status, structure and functions of higher levels of the service and its departmental structure. The commission for problems of contact between the psychological service and public sector["public practice"] of the presidium of the central council of the USSR Society of Psychologists will coordinate and check work dealing with determination of the structure and functions of lower levels of the service and its regional departments.

On the basis of the general objectives, in 1980 the scientific council for problems of applied psychology must prepare goal-oriented programs for development of basic and applied problems of psychology, in order to resolve the immediate and long-range problems of social practice; it should prepare an atlas (reference book) of research and practical work in sectors and agencies; it should define typical problems, status, structure and function of agency services and prepare a draft for the "Psychological service of the USSR." During the same years, it should prepare a draft for development of an instrument and technical-methodological base for the service; it should work out drafts of summary plans

of educational programs and plans for the training and retraining of specialists to meet the needs of the service; it should define the strategy for the next stages of development of the USSR psychological service and its relation to basic science.

The commission under the presidium of the central council of the USSR Society of psychologists will have to prepare a regional atlas (guide) in 1980 of research and practical work in the area of applied psychology (topics, centers, equipment); it must define the typical tasks, directions and specifics of the work of regional and lower levels of the service; it should determine the differentiated requirements (current and future) with regard to psychologists [psychological cadres] in different areas of the national economy. Drafts must be prepared of the typical structure of regional services and their legal-organizational status, as well as drafts of the typical structure of lowest levels of the service, nomenclature of positions, rights and duties of psychologists. In these years, drafts will have to be prepared for curriculums, as well as syllabuses for training psychologists to work in different parts of the public sector ["public practice"].

In 1980-1981, it will be desirable (in the nature of an experiment) to establish two types of psychological service: departmental and regional. The former could be founded on the basis of technical subjects and the latter (at 2-3 scientific-industrial centers, in Moscow, Leningrad, Kurgan) should direct itself to problems of social development and administration (family and domestic services, professional consultations, vocational guidance and vocational "diagnostics," service for social development of groups).

Concrete suggestions on the structure and functions of the experimental services could be prepared by the scientific council and Society of Psychologists in 1980.

On the basis of the experience gained in operating these services, the variants in solving organizational, material, personnel, legal and economic problems of creating a unified psychological service in our country will be analyzed. After summarizing all of the available data and experience gained in operating the experimental services in 1981-1985, the scientific council for problems of applied psychology will have to prepare a comprehensive (complete) draft for the USSR psychological service in 1985.
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PSYCHOPHYSIOLOGICAL BASES OF THE SCIENTIFIC ORGANIZATION OF LABOR

Moscow PSIKHFIZIOLOGICHESKIYE OSNOVY NAUCHNOY ORGANIZATSII TRUDA in Russian 1979 signed to press 12 Mar 79, pp 3-5, 174-175, 176

/Annotation, Introduction and Table of Contents from book by S.A. Kosilov, Moscow "Ekonomika" 1979, 176 pp/

/Text/ This monograph presents discussions of the problem ensuring optimal participation of a worker in a "man-technology" system and an account of peculiarities of physiological functions and mental processes during organization of labor. The author describes the essence of physiological laws of adaptation to labor, their use in designing rational versions of work movements, optimal regimes of work and rest, etc.. A mathematical interpretation of the dynamics of the capacity for work permits a strictly scientific evaluation of the heaviness and intensity of labor for specific sections of production.

The practical recommendations presented in the book were checked under laboratory and production conditions.

It is intended for use by workers of Scientific Organization of Labor services, students and teachers in schools and departments of economics.

Introduction

The USSR Constitution states that the purpose of the state is to provide for the expansion of existing opportunities for the use by citizens of their creative forces, capacities and gifts for the multiform development of the personality. The state is concerned about improvements of the conditions of work and labor protection, the scientific organization of work, the reduction and future elimination of heavy physical labor on the basis of complex mechanization and automation of production processes in all sectors of the national economy.

The creation of favorable conditions of labor, the comprehensive development of the personality and the creative capacities of man require the

consideration of specific laws of adaptation of the human organism to labor and the development, on this base, of measures which permit the optimization of use of the mental and physiological functions of man during work.

The study of the physiological bases of different kinds of physical and mental work and the comprehensive use of the laws of physiology and psychology for improvement of labor processes is the task of the psychophysiology of labor.

In ergonomics and engineering psychology, a "man-tool-work object-production environment system or a "man-machine" system (MMS) is studied as a unified functional entity (analogous to the study of other cybernetic systems). Acknowledgement of the leading role, in this system, of man does not detract from the fact that the coordination of the man-operator with characteristics of machines proceeds mainly on the basis of cybernetics, the theory of probability, mathematical statistics, information theory, mass servicing theory, network planning, reliability theory, etc.. A characteristic (for ergonomics and engineering psychology) digression from complex integration in the work of reflexes, which arise at different levels of the nervous system with the participation of different functions and different analyzers calls for a simplified, uniform component approach to the design and analysis of a man-machine system. "During design and analysis of a man-machine system, the man and the machine are considered as separate links of a system, the analysis and description of which are conducted from unified positions with the use of uniform criteria of evaluation."[1].

The increase of attention and exactingness for the working man does not conform with such an equicomponent approach and places before economists, organizers of labor and production the problem of the study of man at work as a complex, independent system under the command of specific natural and social laws. Characterizing the human system from the position of physiology, I.P. Pavlov indicates that "our system is, to the highest degree, a self-regulating system, maintaining itself, restoring itself, correcting itself and even improving itself."[2]

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1. Engineering Psychology. Edited by G.K. Sereda, Kiev, Vishcha shkola, p 27, 1976.

2. Pavlov, I.P., Complete Collected Works, V 3, Book 2. Moscow-Leningrad, Published by the USSR Academy of Sciences, p 188, 1951.

For rational and complete utilization of the reserves of increase in labor productivity found in the very nature of man, it is obviously insufficient only to enumerate the operations which the working man must perform and to determine the "incoming" and "outgoing" characteristics of the human link in a man-machine system. It is necessary to investigate the dynamics of the functional states of the working man and to analyze the formation by him of a work goal and the form of the necessary work movements, the interaction of physiological functions, which stipulate the active forms of his work behavior.

The comprehensive consideration of physiological and psychological regularities during development of measures for the scientific organization of labor is an important factor in increasing the effectiveness of these measures.

At present, recommendations of the psychophysiology of labor are being used successfully for solution of some important national economic problems. In particular, experience in the use of methods and recommendations of labor physiology at different enterprises of the country for the purpose of substantiating a rational work regime and for increasing the precision of evaluation of its difficulty was used in construction of a universal theory and methods of integral evaluation of the capacity to work during mental and physical work[1] and during development of typical intra-shift regimes of work and rest of industrial workers.[2]

However, a homocentric approach to the scientific organization of labor does not lead to the solution of these problems alone. The development of scientific studies of the psychophysiological possibilities of man for revealing reserves of increase of labor productivity is of great significance. From this point of view, it is necessary to study the development of the capacities of man for work, the physiological processes which participate in changes of the personal nature of the working man. According to the well-known proposition of Marxism, the working man "is acting upon the external environment and changing it at the same time as he is changing his own nature."[3]

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1. See Derevyanko Ye.A. An Integral Evaluation of the Capacity to Work During Mental and Physical Labor. Methodical Recommendations. Moscow, "Economics" 1976.

2. See Derevyanko Ye.A. Typical Inter-Shift Regimes of Work and Rest of Industrial Workers (Intersectoral Methodical Recommendations). Moscow, Scientific Research Institute of Labor, 1977.

3. Marx and Engels. F. Works. 2d edition, V 23, p 188.

In order to control this change of the nature of man in a purposeful and scientifically substantiated manner and the development in the labor processes, ensuing in the organism, in the consciousness of the working person, it is necessary to study how habits are formed in labor, the work movements and the skill to plan work, the mastery and culture of labor. The physiology and psychology of work, developing in close interaction, constitute such a complex study.

This book presents results of contemporary psychophysiological studies of different forms of work activity for purposes of revealing regularities of the increase of the capacity to work and the improvement of the organization of work.

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VII. SCIENCE POLICY AND ADMINISTRATION

ACADEMY OF SCIENCES ANNOUNCES NEW MEMBERS

Moscow VESTNIK AKADEMII NAUK SSSR in Russian No 7, 1979 pp 110-111, 128-130

[Article]

[Excerpts] Academicians

Department of Physiology

Nikolay Nikolayevich Blokhin (Physiology, Oncology)

Born 1912, president of the USSR Academy of Medical Sciences, general director of the USSR Academy of Medical Sciences Oncological Scientific Center, honorary president of the International Anticancer Union, editor in chief of the journal VESTNIK AMN SSSR, specialist in research on malignant tumors, their diagnosis, prevention, and treatment, and author of more than 180 scientific works.

N. N. Blokhin's research centers mainly on biology, biochemistry, virology, and immunology of tumors. He made a great contribution to development of the medicinal method for treating malignant tumors. Medicinal, radiation, and combined treatment methods were developed and introduced, and research on the incidence of malignant tumors in some areas of our country and their relationship to environmental factors was organized under his guidance.

N. N. Blokhin is a Hero of Socialist Labor and a deputy of the USSR Supreme Soviet. He is a member of the academies of sciences of the USA, Poland, and the GDR.

Yevgeniy Ivanovich Chazov (Physiology, Cardiology)

Born 1929, USSR deputy minister of public health, chief of the Main Administration No 4 of the USSR Ministry of Public Health, general director of the All-Union Cardiological Center of the USSR Academy of Medical Sciences, chairman of the All-Union Scientific Cardiological Society and of the Scientific Council on Cardiovascular Diseases, editor in chief of the journal TERAPEVTICHESKIY ARKHIV, specialist in diseases of the cardiovascular system, and the author of more than 240 scientific works.

Ye. I. Chazov's research embraces a broad range of fundamental and applied problems of modern cardiology. He laid the foundation of a new direction in medicine--molecular cardiology. Ye. I. Chazov's works on the pathogenesis, diagnosis, and treatment of cardiac ischemia have been a great contribution to medicine. He was the first to develop and introduce, into

public health practice, a stage-by-stage system for treating patients with myocardial infarctions, one making it possible to return 80 percent of all people suffering myocardial infarctions to work.

Ye. I. Chazov is a Hero of Socialist Labor, he has received the USSR State Prize twice, and he is an honorary member of the GDR Academy of Sciences, the American Heart Association, the Swedish Scientific Medical Society, and the cardiologist societies of the GDR, Hungary, and Bulgaria. He is a deputy of the USSR Supreme Soviet.

Corresponding Members

Department of Biochemistry, Biophysics, and Chemistry of Physiologically Active Compounds

Vladimir Fedorovich Bystrov (Physical Methods of Biopolymer Research)

Born 1935, deputy director of the USSR Academy of Sciences Institute of Bio-Organic Chemistry imeni M. M. Shemyakin, specialist in biopolymer research, and the author of more than 150 scientific works. His activities embrace a broad range of problems in research on the three-dimensional structure of proteinaceous peptide substances. The new principles he developed for the use of physical methods, mainly nuclear magnetic resonance spectroscopy, made a significant contribution to the development of research on the structure of biologically active compounds in connection with the mechanism of their action.

Fundamental research on the structure and functional interactions of peptides and proteins in solutions occupies a central place in the works of V. F. Bystrov. The integrated approach he developed, based on a combination of physical methods and directed protein modification, opened up fundamentally new possibilities for studying the three-dimensional organization and interaction of protein molecules.

The scientist discovered an effective method for differentiating the surfaces of phospholipid membranes on the basis of nuclear magnetic resonance spectrums, and he used this method to conduct a cycle of research on the structure of membranes and on dynamic processes responsible for ion transport and formation of the asymmetrical structure of membranes.

Iosif Isayevich Gitel'zon (Biophysics)

Born 1928, laboratory director at the Physics Institute imeni L. V. Kirenskiy of the Siberian Branch of the USSR Academy of Sciences, a specialist in the biophysics of complex systems, and the author of over 160 scientific works.

I. I. Gitel'zon developed a theory on a three-stage mechanism for hemolysis, which he used to create the erythrogram method, used to differentiate blood cells on the basis of physicochemical, cytochemical, and immunity properties.

He also developed an original direction in bioenergetics--research on the molecular mechanism of bioluminescence: He determined the energy yield of the luminescent channel and the place where it branches off from the respiratory chain, he demonstrated the role of singlet oxygen in the emission mechanism, he isolated the intracellular inhibitor of luciferase and an aldehyde-like factor that associates oxidation of luciferin with emission, and he revealed ultrastructures in photobacterial cells associated with the capability for emission.

I. I. Gitel'zon developed the methodological principles and apparatus for measuring bioluminescence in the sea, and he established the basic laws governing the distribution of bioluminescent potential in the world ocean.

Working together with I. A. Terskov, I. I. Gitel'zon developed the theory and methods of parametric control of biosynthesis, which make it possible to control the biochemical direction and rate of biosynthesis. It was on this basis that he created a highly closed ecosystem and conducted experiments on presence of people in a self-contained ecosystem for a long period of time (up to half a year).

Nikolay Andreyevich Kiselev (Physical Methods of Biopolymer Research)

Born 1928, sector director, USSR Academy of Sciences Institute of Crystallography imeni A. V. Shubnikov, a specialist in electron microscopy of biological macromolecules, and the author of 78 scientific works.

He created new techniques for electron-microscopic investigation of macromolecules, he developed a procedure for interpreting images on microphotographs, and he obtained a number of results of importance to molecular biology and the general theory of macromolecular structure. Thus in particular he experimentally confirmed the existence of three configurational states of RNA depending on the solution conditions. Research on ribosome structure conducted jointly with Academician A. S. Spirin showed that a specifically ordered ribonucleoprotein strand is the basis of ribosome structure.

N. A. Kiselev is conducting expanded research on the structure of plant viruses and the products of their reconstruction. His research on catalase revealed a new type of enzyme crystallization--tubular crystals with walls consisting of a monomolecular layer.

Department of Physiology

Sergey Naumovich Yefuni (Physiology)

Born 1930, section director, USSR Ministry of Public Health All-Union Scientific Research Institute of of Clinical and Experimental Surgery,

chairman of the USSR Academy of Medical Sciences' Commission on the Problem "Hyperbaric Oxygenation," a specialist in a new area of respiratory physiology--hyperbaric oxygenation, and the author of over 100 scientific works.

S. N. Yefuni's research is devoted to the mechanisms behind the effects of high oxygen partial pressures on energy processes in epithelial and collagen-forming cells. His research opened the way for differentiated use of hyperbaric oxygenation to suppress collagen formation and to stimulate repair. S. N. Yefuni shed more light on the toxic action of oxygen and the mechanisms behind phagocytosis and agglutination of formed blood elements, and he revealed the role of the antioxident enzyme superoxide dismutase in failure of an organism's antioxidation defense. He experimentally developed a fundamentally new means of parapulmonary oxygenation using an oxygen microemulsion. Jointly with the section colleagues S. N. Yefuni conducted a cycle of original studies on the biological dependence of the effect of high oxygen partial pressures on the body on various inert gases.

S. N. Yefuni is a recipient of the USSR State Prize.
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